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24 APRIL 1992



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# ***JPRS Report***

# **Science & Technology**

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***Central Eurasia:  
Life Sciences***

# Science & Technology

## Central Eurasia: Life Sciences

JPRS-ULS-92-012

### CONTENTS

24 APRIL 1992

#### Agricultural Science

- Microdroplet Cultivation of Individual Preselected Plant Protoplasts and Fusion Products  
[I.V. Kirichenko, Yu.Yu. Gleba; *BIOPOLIMERY I KLETKA* Jul-Aug 91] ..... 1
- Biogenic Factor-Induced Disease Resistance in Onions  
[G.Yu. Perkovskaya, A.M. Beyder, et al.; *BIOPOLIMERY I KLETKA*, Vol 7 No 4, Jul-Aug 91] ..... 1
- Partial Resistance of Soviet Winter Wheats to Puccinia Persists  
[L.V. Mikityuk, D.A. Solomatin, et al.; *MIKOLOGIYA I FITOPATOLOGIYA*, Vol 25 No 3, May-Jun 91] ..... 1
- Brown Rust Resistance in Selected Wheats  
[L.A. Smirnova, D.A. Solomatin; *MIKOLOGIYA I FITOPATOLOGIYA*, Vol 25 No 3, May-Jun 91] ..... 1
- Somaclonal Variations and Biotechnology of Cereal Improvement  
[A.M. Bondarenko; *FIZIOLOGIYA I BIOKHIMIYA KULTURNYKH RASTENIY*, Vol 23 No 3, May-Jun 91] .... 1

#### Biochemistry

- Interaction of Mouse Organ Cells With Liposomes of Varying Composition  
[G. I. Muzya, L. P. Grabareva, et al.; *BIOKHIMIYA*, Vol 56 No 7, Jul 91] ..... 2
- Lupine Seed Proteins That Bind Molybdenum, Tungsten, and Radionuclides Emitted by the Chernobyl Nuclear Power Plant [K. L. Kaladutskiy, A. I. Zabolotnyy, et al.; *BIOKHIMIYA*, Vol 56 No 7, Jul 91] ..... 2
- Effect of Homobrassinolide, Human Interferon, and (2'-5')-Oligoadenylates on Protein Synthesis in Wheat Leaves  
[E. A. Burkhanova, A. B. Fedina, et al.; *BIOKHIMIYA*, Vol 56 No 7, Jul 91] ..... 2
- Study of the Composition of the Cellulose Fraction of *Colstridium thermocellum*  
[A. V. Bolobova, A. V. Zhukov; *BIOKHIMIYA*, Vol 56 No 7, Jul 91] ..... 2

#### Biophysics

- Model of Ion Channel Formation of Spatial Patterns on the Cell Membrane Surface  
[A. A. Polezhayev and R. A. Saburov; *BIOFIZIKA*, Vol 36 No 5, Sep-Oct 91] ..... 3
- Temperature Dependence of the Conductivity of Single Potential-Dependent K<sup>+</sup>-Channels in Mollusk Neurons  
[V. E. Tseyeb, V. I. Geletyuk, et al.; *BIOFIZIKA*, Vol 36 No 5, Sep-Oct 91] ..... 3
- Biological Activity of Kurilostatin—An Unusual Alkaloid From Sea Sponges  
[A. M. Popov, T. N. Makaryeva, et al.; *BIOFIZIKA*, Vol 36 No 5, Sep-Oct 91] ..... 3
- Change in the Immunogenicity of Cells and the Supernatant Under Ultrasound  
[V. A. Buts, K. P. Skibenko; *BIOFIZIKA*, Vol 36 No 5, Sep-Oct 91] ..... 3

#### Environment

- Features of Nitrate and Nitrite Accumulation in Drinking Water Sources  
[P. D. Klochenko and A. I. Sakevich; *GIGIYENA I SANITARIYA*, No 6, Jun 91] ..... 4

#### Genetics

- Complete Genome Sequence of Eastern Equine Encephalomyelitis Virus (EEEV)  
[V.Ye. Volchkov, V.A. Volchkova, et al.; *MOLEKULARNAYA GENETIKA, MIKROBIOLOGIYA I VIRUSOLOGIYA*, No 5, May 91] ..... 7
- Transposon-Based Studies on Genetics of *Vibrio Cholerae* Non-O1  
[Ye.A. Zhuravleva, N.I. Smirnova, et al.; *MOLEKULARNAYA GENETIKA, MIKROBIOLOGIYA I VIRUSOLOGIYA*, No 5, May 91] ..... 7
- Cloning of Human Prointerleukin-6 Encoding cDNA  
[S.V. Kotenko, N.V. Taranenko, et al.; *MOLEKULARNAYA GENETIKA, MIKROBIOLOGIYA I VIRUSOLOGIYA*, No 5, May 91] ..... 7

#### Immunology

- Diagnosis of Tick-Borne Encephalitis (TBE) By Indirect Immune Rosette Formation (IIRF)  
[L.P. Bykova, V.M. Minayeva, et al.; *ZHURNAL MIKROBIOLOGII, EPIDEMIOLOGII I IMMUNOBIOLOGII*, No 5, May 91] ..... 8
- Detection of IgM by Enzyme Immunoassay (EIA) and Passive Hemagglutination (PH) in Diagnosis of Tick-Borne Encephalitis (TBE)  
[Ye.V. Kudrevatykh, R.Z. Kuzyayev, et al.; *ZHURNAL MIKROBIOLOGII, EPIDEMIOLOGII I IMMUNOBIOLOGII*, No 5, May 91] ..... 8
- Opioid Binding Immunoglobulins in Atopic Dermatitis and Drug Addiction  
[O.Yu. Polevaya, V.A. Samsonov, et al.; *IMMUNOLOGIYA*, No 2, Feb 91] ..... 8

|   |    |
|---|----|
| Indicators of Nonspecific Resistance in HIV Infections<br>[A.G. Rakhmanova, V.A. Isakov, et al.; IMMUNOLOGIYA, No 2, Feb 91]  | 8  |
| <b>Medicine</b>   |    |
| Immunoadsorption Therapy for AIDS<br>[B.A. Shmatkov, D.V. Kulayev; ZHURNAL MIKROBIOLOGII, EPIDEMIOLOGII I IMMUNOBIOLOGII, No 5, May 91]   | 9  |
| Evaluation of Effectiveness of Influence of Magnetic Eddy Field on Course of Tumor Process in Generalized Cancer of the Mammary Gland<br>[N. G. Bakhmutskiy, T. A. Pyleva; SOVETSKAYA MEDITSINA, No 7, Jul 91]  | 9  |
| Use of Antioxidants in Treatment of Vibration Sickness<br>[V. G. Artamonova, L. V. Kuskova; GIGIYENA TRUDA I PROFESSIONALNYE ZABOLEVANIYA, No 4, Apr 91]  | 9  |
| Acute Occupational Poisoning in Closed Spaces<br>[V. A. Meleshchenko, V. A. Mikheyev; GIGIYENA TRUDA I PROFESSIONALNYE ZABOLEVANIYA, No 4, Apr 91]  | 9  |
| <b>Microbiology</b>   |    |
| Effect of Industrial Air Pollution on Soil Microbiology<br>[V.P. Stefurak; MIKROBIOLOGICHESKIY ZHURNAL, Vol 53 No 6, Nov-Dec 91]  | 10 |
| Comparative Assessment of Serologic Diagnosis of Epidemic Typhus<br>[Yu.A. Nedyalkov, E.I. Drobyshevskaya, et al.; ZHURNAL MIKROBIOLOGII, EPIDEMIOLOGII I IMMUNOBIOLOGII, No 5, May 91]   | 10 |
| Conjugative Transfer of Sa Plasmid Via Recombinant pSKEFT5 Plasmid From Escherichia Coli to Francisella Tularensis<br>[A.P. Pomerantsev, I.V. Domaradskiy, et al.; MOLEKULARNAYA GENETIKA, MIKROBIOLOGIYA I VIRUSOLOGIYA, No 5, Aug 91]               | 10 |
| Protein Expression in Long-Term in Vivo Culture of Yersinia Pestis<br>[G.Yu. Kulyash, Ye.M. Golovko, et al.; MOLEKULARNAYA GENETIKA, MIKROBIOLOGIYA I VIRUSOLOGIYA, No 5, Aug 91]   | 10 |
| Seventh Cholera Pandemic in the World and USSR<br>[M. I. Narkevich, G. G. Onishchenko, et al.; ZHURNAL MIKROBIOLOGII, EPIDEMIOLOGII I IMMUNOBIOLOGII, No 6, Jun 91]   | 10 |
| Cholera-Control Measures Implemented in the USSR During Seventh Cholera Pandemic<br>[M. I. Narkevich, G. G. Onishchenko, et al.; ZHURNAL MIKROBIOLOGII, EPIDEMIOLOGII I IMMUNOBIOLOGII, No 6, Jun 91]   | 14 |
| Cloning and Detailed Mapping of Fra-Ymt Region of Plasmid pFra of Yersinia Pestis<br>[P.A. Cherepanova, T.G. Mikhaylova, et al.; MOLEKULARNAYA GENETIKA, MIKROBIOLOGIYA I VIRUSOLOGIYA, No 5, Aug 91]   | 17 |
| Temperate SM Phage of Pseudomonas Aeruginosa as Cloning Vector<br>[A.M. Kulba, A.S. Gorelyshev, et al.; MOLEKULARNAYA GENETIKA, MIKROBIOLOGIYA I VIRUSOLOGIYA, No 5, Aug 91]  | 18 |
| <b>Pharmacology, Toxicology</b>   |    |
| Suppression of Cellular Na <sup>+</sup> /H <sup>+</sup> Metabolism Inhibits Influenza Virus Activity<br>[V. A. Kirillov, L. N. Goreva, et al.; ANTIBIOTIKI I KHIMIOTERAPIYA, Vol 36 No 6, Jun 91]   | 19 |
| Multifactorial Analysis of Combined Effect of Antibiotic and Low Molecular Weight Microbial Origin Immunostimulant on Experimental Plague Infection<br>[A. V. Nikitin, L. N. Makarovskaya, et al.; ANTIBIOTIKI I KHIMIOTERAPIYA, Vol 36 No 6, Jun 91] | 19 |
| Salts of $\beta$ -Glycyrrhizic Acid—Stimulators of Reparative Skin Regeneration<br>[V. A. Davydova, T. G. Tolstikova, et al.; KHIMIKO-FARMATSEVTICHESKIY ZHURNAL, Vol 25 No 5, May 91]  | 19 |
| Synthesis and Antiviral Activity of 3-Cyano-2(1H)-pyridine Selenones<br>[V. Yu. Mortikov, V.P. Livinov, et al.; KHIMIKO-FARMATSEVTICHESKIY ZHURNAL, Vol 25 No 5, May 91]  | 20 |
| Antiviral Activity of Macrocyclic Polyethers and Their Complexes With Alkaline Salts of N-Phosphorylated Amides and Thioamides<br>[N. G. Zabirow, O. K. Pozdeyev, et al.; KHIMIKO-FARMATSEVTICHESKIY ZHURNAL, Vol 25 No 5, May 91]                    | 20 |
| Computer Prediction and Study of Biological Properties of Nitrofurlylvinyl (Polyenyl) Quinolones<br>[A. Rozenblit, V. Golender, et al.; KHIMIKO-FARMATSEVTICHESKIY ZHURNAL, Vol 25 No 5, May 91]  | 20 |
| Effect of Certain Fluids and Steam Sterilization on Strength Properties of Polyamide Membranes<br>[G. B. Bochkova, A. S. Yushin; KHIMIKO-FARMATSEVTICHESKIY ZHURNAL, Vol 25 No 5, May 91]   | 20 |

|  |    |
|--|----|
| Synthesis and Assessment of Nitrogen-Containing Adamantane Derivatives<br>[Yu. N. Klimochkin, I. K. Moiseyev, et al.; <i>KHIMIKO-FARMATSEVTICHESKIY ZHURNAL</i> , Vol 25 No 7, Jul 91]   | 21 |
| Synthesis and Assessment of Sulfur-Containing Adamantane Derivatives<br>[Yu. N. Klimochkin, I. K. Moiseyev, et al.; <i>KHIMIKO-FARMATSEVTICHESKIY ZHURNAL</i> , Vol 25 No 7, Jul 91]   | 21 |
| <b>Physiology</b>  |    |
| Effects of Opiate Agonists on Myocardial Energetics in Rats With Hemorrhagic Shock<br>[V. D. Slepishkin, Yu. Gressler; <i>BYULLETen EKSPERIMENTALNOY BIOLOGII I MEDITSINY</i> , Vol 111 No 5, May 91]  | 22 |
| Facilitated Extinction of Exploratory Activity as Indication of Nootropic Action<br>[R. U. Ostrovskaya, T. A. Gudasheva; <i>BYULLETen EKSPERIMENTALNOY BIOLOGII I MEDITSINY</i> , Vol 111 No 5, May 91]  | 22 |
| Experimental Assessment of Oxygen Capacity of Modified Polyhemoglobin in Extreme Dilution Models<br>[I. R. Kolonina, Yu. A. Litvinenko, et al.; <i>BYULLETen EKSPERIMENTALNOY BIOLOGII I MEDITSINY</i> , Vol 111 No 5, May 91]   | 22 |
| Intracerebral Microdialysis in Assessment of Effects of Atypical Neuroleptics and Anxiolytics on Release and Metabolism of Striatal Dopamine in Wakeful Rats<br>[M. B. Bogdanov, R. R. Faynetdinov, et al.; <i>BYULLETen EKSPERIMENTALNOY BIOLOGII I MEDITSINY</i> , Vol 111 No 5, May 91] | 22 |
| <b>Public Health</b>   |    |
| Revitalization of Pharmaceutical Industry Urged [N. Dmitriyeva; <i>DELOVOY MIR</i> 4 Dec 92]   | 23 |
| Pigment Used As Radiation Injury Treatment [M. Nikolayeva; <i>ROSSIYSKAYA GAZETA</i> 16 Jan 92]  | 24 |
| Stress Epidemic in Chernobyl Victims [I. Brekhman; <i>PRAVDA</i> 14 Dec 92]  | 24 |
| <b>Radiation Biology</b>   |    |
| Biological Aspects of Low-Dose Radiation<br>[V. Ya. Gotlib, I. I. Pelevina, et al.; <i>RADIOBIOLOGIYA</i> , Vol 31 No 3, May-Jun 91]   | 26 |
| <b>Virology</b>  |    |
| Polymeric Peptide Vaccine Against Foot-and-Mouth Disease Virus<br>[A. V. Pavlov, S. S. Rybakov, et al.; <i>BIOORGANICHESKAYA KHIMIYA</i> , Vol 17 No 7, Jul 91]  | 27 |
| Cloning of Streptococcus bovis $\alpha$ -Amylase Gene and Its Expression in <i>Bacillus subtilis</i> Cells<br>[P. Yavorski, M. M. Kuntsova, et al.; <i>MOLEKULYARNAYA GENETIKA, MIKROBIOLOGIYA I VIRUSOLOGIYA</i> , No 6, Jun 91]  | 27 |
| Investigation of Antigenic Structure of Glycoprotein E1 From Venezuelan Equine Encephalomyelitis Virus Using Monoclonal Antibodies<br>[I. A. Razumov, Ye. V. Agapov, et al.; <i>MOLEKULYARNAYA GENETIKA, MIKROBIOLOGIYA I VIRUSOLOGIYA</i> , No 6, Jun 91]                                 | 27 |
| Conjugation and Microencapsulation of Antigens [VOPROSY VIRUSOLOGII, Vol 36 No 4, Jul-Aug 91]  | 28 |
| Miscellaneous  | 28 |
| Photometric Determination of Sodium and Cesium Iodides in Workplace Air<br>[A. V. Gorelova, I. L. Gerasimova, et al.; <i>GIGIYENA TRUDA I PROFESSIONALNYYE ZABOLEVANIYA</i> , No 9, Sep 91]  | 28 |
| Gas-Chromatographic Determination of Dichlorpinacolin in Workplace Air and in Water<br>[Kh. T. Asilbekova, V. M. Khasanova; <i>GIGIYENA TRUDA I PROFESSIONALNYYE ZABOLEVANIYA</i> , No 9, Sep 91]  | 29 |



### Microdroplet Cultivation of Individual Preselected Plant Protoplasts and Fusion Products

927C0310A Kiev BIOPOLIMERY I KLETKA in Russian Vol 7 No 4, Jul-Aug 91 (manuscript received 14 Jan 91) pp 6-20

[Article by I.V. Kirichenko and Yu.Yu. Gleba, Institute of Cellular Biology and Genetic Engineering, Ukrainian SSR Academy of Sciences, Kiev; UDC 578.085]

[Abstract] Technical aspects of microdroplet cultivation of preselected individual plant protoplasts and electrofusion products are presented in combination of a review of existing technologies. Current experience shows that under optimum conditions plating efficiencies vary widely depending on the species, from a low of 2 percent for clover to a high approaching 75 percent for tobacco. Replenishment with appropriate fresh medium has been shown to be significant factor in enhancing efficiency. Certain media were also identified as favoring electrofusion, yielding efficiencies on the order of 95 percent in the case tobacco plants. Figures 7; tables 4; references 41: 2 Ukrainian, 4 Russian, 35 Western.

### Biogenic Factor-Induced Disease Resistance in Onions

927C0310B Kiev BIOPOLIMERY I KLETKA in Russian Vol 7 No 4, Jul-Aug 91 (manuscript received 14 Jan 91) pp 91-94

[Article by G.Yu. Perkovskaya, A.M. Beyder and A.P. Dmitriyev, Institute of Cellular Biology and Genetic Engineering, Kiev; Ukrainian Scientific Research Institute of Vegetable and Cucurbit Farming, Ukrainian SSR State Agricultural Industry, Kharkov; UDC 577.1.11:632.938]

[Abstract] Research on elicitors of plant resistance to disease involved GLC analysis of fatty acids of alcoholic extracts of *Botrytis allii* mycelia. The results demonstrated the presence of  $C_{18}$  and  $C_{20}$  unsaturated fatty acids, with linoleic and linolenic acids representing 1/3rd of the total. Pretreatment of onion seeds with the extract ( $10E-6$  M; identified as the Soviet preparation Linetol) and, for comparison, with arachidonic acid ( $10E-7$  M) reduced the rates of infection with peronosporosis [as published] by 59.6 and 57.6 percent, respectively. Accordingly, the lipid fraction of *B. allii* has been shown to contain fatty acids that function as systemic, nonspecific elicitors in analogy to arachidonic acid. Tables 3; references 8: 7 Russian, 1 Western.

### Partial Resistance of Soviet Winter Wheats to Puccinia Persistens

927C0323A Leningrad MIKOLOGIYA I FITOPATOLOGIYA in Russian Vol 25 No 3, May-Jun 91 (manuscript received 20 Jul 90) pp 244-249

[Article by L.V. Mikityuk, D.A. Solomatin, Ye.N. Artemenko and D.I. Chkanov, All-Union Scientific Research Institute of Phytopathology, Moscow Oblast; UDC 633.11:632.938:582.285.2]

[Abstract] Field and laboratory studies were conducted on seven varieties of Soviet winter wheat to determine their partial resistance to brown rust (*Puccinia persistens*). The results led to identification of Prikubanskaya and Polesskaya Bezostaya wheats as meeting acceptable resistance criteria under both field and laboratory conditions. The findings indicated that such factors as latent period of infection, leaf receptivity and enumeration of mycelia are equally valid in evaluation of partial resistance. Prikubanskaya and Polesskaya Bezostaya evidenced equivalent degrees of resistance to *P. persistens* biotypes 25, 52 and 77. Tables 5; references 10: 6 Russian, 4 Western.

### Brown Rust Resistance in Selected Wheats

927C0323B Leningrad MIKOLOGIYA I FITOPATOLOGIYA in Russian Vol 25 No 3, May-Jun 91 (manuscript received 27 Jun 90) pp 253-257

[Article by L.A. Smirnova and D.A. Solomatin, All-Union Scientific Research Institute of Phytopathology, Moscow Oblast; UDC 633.11:582.285.2:632.938]

[Abstract] An analysis was conducted on partial resistance in selected winter and spring wheats cultivated in the USSR to various biotypes of the leaf rust agent *Puccinia recondita*. The results demonstrated that both kinds of wheat evidenced partial resistance, but that partial resistance was much more frequent in winter wheats. Partial resistance in Soviet wheats is largely due to extensive use of American varieties (Americano 44d, Klein 33, Klein Rendidor) for breeding purposes in the fifties. The same strategy can be used to introduce the partial resistance trait more widely into spring wheats and extend the usefulness of *Lr* genes. Figures 2; tables 3; references 6: 3 Russian, 3 Western.

### Somaclonal Variations and Biotechnology of Cereal Improvement

927C0323C Kiev FIZIOLOGIYA I BIOKHIMIYA KULTURNYKH RASTENIY in Russian Vol 23 No 3, May-Jun 91 (manuscript received 25 Oct 90) pp 222-232

[Article by A.M. Bondarenko, Institute of Plant Physiology and Genetics, Ukrainian SSR Academy of Sciences, Kiev; UDC 581.143.6]

[Abstract] A review of predominantly Western literature is presented on the biotechnology of cereal improvement and somaclonal variations. Research to date shows that callus formation, cell growth under in vitro culture conditions, and regeneration of somaclonal plants are under fine genetic control. In order to optimize these various efforts at cereal grain improvement, a better understanding of the genetic control mechanisms is required in addition to definition of biochemical and physiological features. The demonstration that chemical mutagenesis can be utilized for manipulation of callusogenesis, cell reproduction and regeneration of somaclonal plants demonstrates that in vitro chemical mutagenesis represents one of the more promising avenues for engineering improved crops. References 102: 39 Russian, 63 Western.

**Interaction of Mouse Organ Cells With Liposomes of Varying Composition**

927C0276A Moscow BIOKHIMIYA in Russian Vol 56  
No 7, Jul 91 (manuscript received 16 Jul 90, after revision  
14 Dec 90) pp 1215-1219

[Article by G. I. Muzya, L. P. Grabareva, L. N. Dmitriyeva, K. P. Kashkin, and V. I. Kulikov; Scientific-Production Center for Medical Biotechnology, USSR Ministry of Public Health, Moscow; UDC 577.125]

[Abstract] The distribution of liposomes, obtained from total mouse liver lipids and containing  $^3\text{H}$ -labeled thrombocyte activation factor, in mice was studied in this work. It was shown that the major portion of liposomes of the indicated lipid composition was transported to the animals' liver and spleen. The interaction of liposomes of varying lipid composition with spleen cells was studied. It was determined that the affinity of liposomes obtained from macrophage or mouse spleen lymphocyte lipids to mouse spleen cells was significantly higher than the affinity of liposomes obtained from the model liposome mixture. In the overall population of spleen cells, macrophage or lymphocyte binding of liposomes was significantly lower than isolated macrophage or lymphocyte binding of liposomes. References 16: 10 Russian, 6 Western.

**Lupine Seed Proteins That Bind Molybdenum, Tungsten, and Radionuclides Emitted by the Chernobyl Nuclear Power Plant**

927C0276B Moscow BIOKHIMIYA in Russian Vol 56  
No 7, Jul 91 (manuscript received 31 Jul 90, after revision  
21 Jan 91) pp 1220-1227

[Article by K. L. Kalakutskiy, A. I. Zabolotnyy, and N. P. Lvov; Institute of Biochemistry imeni A. N. Bakh, USSR Academy of Sciences, Moscow; Institute of Experimental Botany imeni V. F. Kuprevich, Belorussian SSR Academy of Sciences, Minsk; UDC 577.122]

[Abstract] In this work, two proteins and a low molecular weight fraction that exhibited a capability to bind Mo, W, and radionuclides emitted by the Chernobyl Nuclear Power Plant *in vivo* and the isotope  $^{185}\text{W}$  *in vitro* were identified in seeds from the yellow lupine. The indicated proteins differed in their electrophoretic mobilities. The protein with lower electrophoretic mobility underwent proteolytic degradation where the proteolysis product retained the capability to bind the microelement. Figures 3; references 14: 4 Russian, 10 Western.

**Effect of Homobrassinolide, Human Interferon, and (2'-5')-Oligoadenylates on Protein Synthesis in Wheat Leaves**

927C0276C Moscow BIOKHIMIYA in Russian Vol 56  
No 7, Jul 91 (manuscript received 6 Sep 90), pp 1228-1240

[Article by E. A. Burkhanova, A. B. Fedina, N. V. Danilova, I. B. Kaplan, M. E. Talyanskiy, I. G. Atabekov, and O. N. Kulayeva; Institute of Plant Physiology imeni K. A. Timiryazev, USSR Academy of Sciences, Moscow; Virology Division, Biology Department, Moscow State University imeni M. V. Lomonosov; UDC 578.245]

[Abstract] A comparative study of the effects of (22S,23S)-homobrassinolide (HB), human leucocyte interferon (HLI),

and (2'-5')-oligoadenylates (2,5-A) (mediators of HLI activity in animal cells) on protein synthesis in Saratovskaya 29 variety wheat leaves was conducted at normal temperature and under heat shock (HS) in order to elucidate the molecular mechanisms of the compounds' activities. It was shown that HB, HLI, and 2,5-A activated the accumulation of [ $^{35}\text{S}$ ] methionine in leaf segments and operation of the protein-synthesizing apparatus of cells. More active operation of the protein-synthesizing system under HS conditions allowed the authors to hypothesize about the leaves' increased thermal resistance under the influence of the studied substances. Homobrassinolide, HLI, and 2,5-A changed the spectra of synthesized proteins, which indicated a reprogramming of genome expression. Two-dimensional electrophoresis of the labeled proteins showed that HLI and 2,5-A caused similar changes in the spectrum of synthesized polypeptides at normal temperature and under HS, whereas both similarity and specific differences were found between HB activity and the activities of HLI and 2,5-A. The conducted investigation has opened the field for further study of the roles of HLI, 2,5-A, and HB in reprogramming the genome of plants and in increasing the specificity and overall resistance of plants to stress factors and viral infection. Figures 3; references 22: 5 Russian, 17 Western.

**Study of the Composition of the Cellulosome Fraction of *Clostridium thermocellum***

927C0276D Moscow BIOKHIMIYA in Russian Vol 56  
No 7, Jul 91 (manuscript received 1 Nov 90, after revision  
17 Jan 91) pp 1304-1311

[Article by A. V. Bolobova and A. V. Zhukov; Institute of Biochemistry imeni A. N. Bakh, USSR Academy of Sciences, Moscow; Institute of Plant Physiology imeni K. A. Timiryazev, USSR Academy of Sciences, Moscow; UDC 577.1]

[Abstract] Cellulases in thermophilic bacteria conduct biodegradation of insoluble substrates in nature either by the activity of individual enzymes or by the activity of cellulosomes—intricately organized multiple enzyme complexes having a specific super-molecular structure. In this work, a gel-chromatograph fractionation of the cellulase complex (cellulosome) from *Clostridium thermocellum* was conducted, a relationship between the molecular weight of the cellulosome formations and their cellulolytic activity was established, and the composition of the two major high molecular weight fractions was studied. It was shown that besides protein, the cellulosome contained  $\text{Ca}^{2+}$  ions and a lipid component, containing cardiolipin, 1,2- and 1,3-diglycerides, triglycerides, and fatty acids. A correlation was established between the size of the cellulosome and its lipid and calcium contents. Removal of the extractable lipid portion led to partial decomposition of the cellulosomes. The lipid component of the cellulosomes was identified in the cellulosome portion firmly sorbed to microcrystalline cellulose. It was hypothesized that cellulosomes are calcium-activated phospholipid-dependent protein formations. Figures 3; references 12: 7 Russian, 5 Western.

### Model of Ion Channel Formation of Spatial Pattern on the Cell Membrane Surface

927C0280A Moscow BIOFIZIKA in Russian Vol 36 No 5, Sep-Oct 91 (manuscript received 22 Jun 90) pp 805-809

[Article by A. A. Polezhayev and R. A. Saburov, Physics Institute imeni P. M. Lebedev, Moscow]

[Abstract] In this work, a bifurcational analysis was conducted of the model of ion channel self-organization on the cell membrane surface. It was shown that a region exists in parametric space that corresponds to the mild generation of a stable, nonhomogeneous, spatial pattern. The pattern's formation was initiated by the conjugation of electric charge transport processes and ion channels along the cell membrane. This result allowed the authors to evaluate the role of nonlinear reactions in self-regulating systems in a new way. It is known that for a diffusion instability to arise in a distributed dynamic system, the presence of two spatial quantities where positive feedback operates on the lesser of these, e.g., autocatalysis, is required. The latter is impossible in a system reacting by a mono- or bimolecular mechanism, i.e., in a system with quadratic nonlinearity, which, together with the new structure's required stability, leads to a conclusion about the determining role of cubic (or higher order) nonlinearity. References 5: 4 Russian, 2 Western.

### Temperature Dependence of the Conductivity of Single Potential-Dependent K<sup>+</sup>-Channels in Mollusk Neurons

927C0280B Moscow BIOFIZIKA in Russian Vol 36 No 5, Sep-Oct 91 (manuscript received 5 Feb 91) pp 810-821

[Article by V. E. Tseyeb, V. I. Geletyuk, and V. N. Kazachenko; Institute of Cell Biophysics, USSR Academy of Sciences, Pushchino, Moscow Oblast]

[Abstract] The temperature dependence of the chord conductivity of single potential-dependent fast and slow K<sup>+</sup>-channels was studied by the patch method (inside-out configuration) in the neurons of the freshwater mollusk *Lymnaea stagnalis*. It was established that in the control conditions (20° C, 0 mV, [K<sup>+</sup>]<sub>o</sub>=1.5 mM, [K<sup>+</sup>]<sub>i</sub>=100 mM), the conductivities of the fast and slow K<sup>+</sup>-channels were equal to 20-25 and 30-40 pS, respectively. Additionally, the temperature dependence of currents in low conductivity K<sup>+</sup>-channels (5-20 pS) was studied. It was shown that several of these channels can be investigated as subtypes of fast and slow K<sup>+</sup>-channels. It was established that for all channels, the current (and conductivity) increased with increased temperature; however, in the interval 10-20°C, anomalous current behavior was observed (the current either did not change or even decreased with increased temperature), which may have been due to phase transitions in the membrane. It was shown that outside the limits of the anomalous zone, the temperature dependence of current could be approximated in Arrhenius coordinates by straight lines whose slopes determined the apparent activation energies of channel conductivity ( $\Delta E_a$ ). It was found that for all channels, except the fast ones, at temperatures above 20° C,  $\Delta E_a$  was approximately equal to 16.7 kJ/mol and corresponded to the free diffusion of ions in aqueous solution. For the given temperatures,  $\Delta E_a$  was weakly dependent on the membrane potential; at temperatures below 10° C, the potential dependence of  $\Delta E_a$  for slow K<sup>+</sup>-channels was

significant and observed primarily in the range -20 to 20 mV (the average  $\Delta E_a$  was approximately 50.2 kJ/mol); the potential dependence of  $\Delta E_a$  for low-conductivity channels was weaker. The temperature dependencies of currents in fast K<sup>+</sup>-channels were to a certain degree opposite to analogous dependencies for slow K<sup>+</sup>-channels. Figures 9; references 21: 7 Russian, 14 Western.

### Biological Activity of Kurilostatin—An Unusual Alkaloid From Sea Sponges

927C0280C Moscow BIOFIZIKA in Russian Vol 36 No 5, Sep-Oct 91 (manuscript received 2 Nov 90) pp 830-832

[Article by A. M. Popov, T. N. Makaryeva, and V. A. Stonik; Pacific Ocean Institute of Bioorganic Chemistry, Far East Department of the USSR Academy of Sciences, Vladivostok]

[Abstract] Recently, Japanese authors extracted two alkaloids (prianosines A and B) from the Okinawa sponge *Prianos melanos* that exhibit powerful cytostatic activity against tumor cells *in vitro*. Prianosine A was found to be more active than prianosine B against mouse leucosis cells. Other authors independently extracted alkaloids (discorabidines A, B, C, and D) from *Latrunculia* species sponges as basic pigments. Discorabidine A turned out to be identical to prianosine A. In this work, the authors extracted a natural dark red compound from *Latrunculia* species sponges which they named kurilostatin. The authors studied the activity of kurilostatin on tumor cells, lymphocytes, erythrocytes, and lecithin-cholesterol liposomes. It was shown that the compound exhibited a powerful cytostatic activity against tumor cells and mitogen-activated lymphocytes, but it did not exhibit anti-tumor activity *in vivo*. It was determined that kurilostatin induces the release of free calcium from cells, which may be the basis of its cytostatic effect. Kurilostatin also exhibited antimicrobial activity. Figures 1; references 8: 3 Russian, 5 Western.

### Change in the Immunogenicity of Cells and the Supernatant Under Ultrasound

927C0280D Moscow BIOFIZIKA in Russian Vol 36 No 5, Sep-Oct 91 (manuscript received 21 Jun 90) pp 863-865

[Article by V. A. Buts and K. P. Skibenko; Kharkov Physico-Technical Institute]

[Abstract] The causes of changes in the antigen activity of erythrocytes remain an unsolved problem: do they involve a simple breaking away of surface antigens and development of a new antigen layer, a breaking away of saccharide residues from the glycoprotein, or both simultaneously. This work was conducted to elucidate the causes. It was shown that upon subjecting cells to low and medium intensity ultrasound ( $I = 0.5-3 \text{ W/cm}^2$ ), a portion of the antigens made a transition from the cell surface to the liquid medium surrounding the cells. It was also shown that the immunogenicity of surface antigens (SA), obtained after sonicating the cells (with subsequent centrifugation to separate cells from SA), was no lower than the cells' immunogenicity. References 6: 5 Russian, 1 Western.



### Features of Nitrate and Nitrite Accumulation in Drinking Water Sources

927C0325A Moscow GIGIYENA I SANITARIYA  
in Russian No 6, Jun 91 pp 17-20

[Article by P. D. Klochenko and A. I. Sakevich; UDC 614.777:[628.191:[546.175+546.173]

[Text] Among nitrogen-containing compounds responsible for the biological fitness of water for human consumption, nitrates and their reduction products—nitrites—are the most important. It was established<sup>1,8</sup> that they are precursors of carcinogenic N-nitroso compounds, and that they reduce the body's resistance to mutagenic and carcinogenic factors. Excess quantities of nitrates in drinking water change its organoleptic properties and cause development of methemoglobinemia ("cyanosis") in animals and man<sup>2,9,11</sup>.

Contamination of drinking water supply sources (reservoirs, rivers, lakes, wells) by nitrates is presently associated with inflow of liquid industrial, municipal and domestic wastes, runoff from agricultural land and processes occurring within the water basin<sup>7</sup>.

The goal of this research was to study the features of accumulation of nitrates and nitrites in different types of drinking water sources.

Water samples were taken in different seasons of the year from Dniepr reservoirs, their tributaries and wells located in the vicinity of the Dniepr basin. Nitrates and nitrites were determined in accordance with the procedure in<sup>10</sup>. Algal biomass was established by volumetric calculation<sup>4</sup>.

According to published data<sup>3</sup> the concentration of nitrites in water of Dniepr reservoirs basically does not exceed thousandths and hundredths of a milligram per liter, and in rare cases it increases to tenths, while the concentration of nitrates may vary from 0 to several milligrams. Our research

showed that the nitrate concentration in Dniepr reservoirs was within 0-2.01 mg N/liter, and that of nitrites was 0-0.152 N/liter (Table 1).

**Table 1. Variation Limits of Nitrate and Nitrite Concentrations (mg N/liter) in Water of Dniepr Reservoirs in 1982-1989**

| Reservoir        | Nitrates  | Nitrites    |
|------------------|-----------|-------------|
| Kiev             | 0.06-1.56 | 0-0.025     |
| Kanav            | 0-1.02    | 0-0.057     |
| Kremenchug       | 0-1.51    | 0-0.020     |
| Dneprodzerzhinsk | 0-1.03    | 0-0.020     |
| Zaporozhye       | 0.16-1.52 | 0.003-0.153 |
| Kakhovka         | 0.02-1.88 | 0-0.024     |

The concentration of nitrate and nitrite nitrogen in reservoirs varies within wide limits in relation to season, water basin and depth, as well as between shallow and deep regions.

Maximum accumulation of nitrates and nitrites is characteristic of reservoirs in winter and early spring, when the intensity of biological processes weakens. With the onset of summer the concentration of nitrite and nitrate nitrogen decreases noticeably, and sometimes attains analytical zero. This is associated chiefly with intensive development of phytoplankton, which is responsible for the distribution of the compounds in question through the water basin. In most cases the concentration of nitrate and nitrite nitrogen decreases from upstream regions to regions near dams (Table 2). Kakhovka Reservoir, where massive development of blue-green algae, and primarily *Microcystis aeruginosa*, was noted in the middle and partly in the upper regions of the reservoir, was an exception.

**Table 2. Variation Limits of the Concentrations of Nitrates, Nitrites (mg N/liter) and Phytoplankton (mg/liter) in Some Regions of Dniepr Reservoirs in Summer 1984-1985**

| Reservoir   | Nitrates  | Nitrites    | Algal Biomass |
|-------------|-----------|-------------|---------------|
| Kiev:       |           |             |               |
| upper part  | 0.11-0.46 | 0.009-0.016 | 2.8-14.7      |
| lower part  | 0.06-0.10 | 0-0.005     | 18.2-2,707.9  |
| Kremenchug: |           |             |               |
| upper part  | 0.09-0.51 | 0.006-0.018 | 0.3-8.2       |
| middle part | 0.03-0.20 | 0-0.015     | 0.8-13.7      |
| lower part  | 0-0.10    | 0-0.008     | 8.1-38.9      |
| Kakhovka:   |           |             |               |
| upper part  | 0.05-0.29 | 0.005-0.007 | 1.3-17.2      |
| middle part | 0.02-0.13 | 0-0.008     | 76.0-105.0    |
| lower part  | 0.05-0.33 | 0.007-0.024 | 0.8-7.7       |

The depth distribution of nitrites and nitrates is also associated to a significant degree with development of phytoplankton, the biomass and functional activity of which is higher as a rule in the surface layers. This is especially noticeable in the period of still weather in summer.

It can be noted in regard to shallow and deep zones that because of the lack of oxygen, biogenic forms of nitrogen— $\text{NO}_2^-$  and  $\text{NO}_3^-$ —are found in the waters of shallow zones in negligible quantities as compared to deep zones, and sometimes they are completely absent<sup>6</sup>. In some cases active development of macrophytes promotes this as well.

Phytoplankton (chiefly blue-green algae) developing intensively in reservoirs is also a source supplying nitrate and nitrite nitrogen upon die-off and bacterial decomposition of algal cells<sup>5</sup>. The concentration of mineral forms of nitrogen in decomposing accumulations of blue-green algae (bloom patches) may increase by five to 10 times in comparison with that in areas of water containing algae with no signs of decomposition. An example of this in our research is some regions of Kremenchug Reservoirs (Adamovskaya Bay), where the nitrate concentration did not fall below 0.22 mg N/liter at an algal biomass of 22,500 mg/liter. In the case of Kakhovka Reservoir, we noted such a phenomenon in the vicinity of the town of Blagoveshchenki, where the biomass of *M. aeruginosa* blue-green algae was 16,380 mg/liter and the concentration of nitrates in water was 0.13 mg N/liter.

The Bortnicheskaya aeration station can be named among allochthonous sources of enrichment of Dniepr water with nitrogen compounds. The outflow from this facility contained up to 0.37 mg N/liter nitrites and 3.95 mg N/liter nitrates.

The Dniepr's tributaries are subjected to the greatest anthropogenic influence, as is evidenced by the levels of accumulation of nitrate and nitrite nitrogen in them (Table 3).

**Table 3. Variation Limits of Nitrate and Nitrite Concentrations (mg N/liter) in Water of Dniepr Tributaries in 1982-1989**

| River        | Nitrates  | Nitrites    |
|--------------|-----------|-------------|
| Pripyat      | 0-1.07    | 0.004-0.014 |
| Teterev      | 0.17-1.33 | 0.007-0.029 |
| Zdvizh       | 0-7.30    | 0.005-0.036 |
| Irpen        | 0-1.32    | 0.002-0.058 |
| Desna        | 0.29-1.53 | 0-0.031     |
| Lybid        | 0.90-1.96 | 0.065-0.300 |
| Stugna       | 0.64-2.50 | 0.007-0.022 |
| Krasnaya     | 0.28-0.42 | 0.013-0.022 |
| Trubezh      | 0.13-1.39 | 0.005-0.056 |
| Ros          | 0-1.90    | 0-0.022     |
| Rosava       | 0.41-1.50 | 0.011-0.017 |
| Olshanka     | 0-1.70    | 0-0.021     |
| Sula         | 0-0.29    | 0-0.007     |
| Tyasmin      | 0-3.10    | 0-0.037     |
| Tsybulnik    | 0-1.29    | 0-0.036     |
| Psel         | 0.31-2.80 | 0.005-0.014 |
| Vorskla      | 0.08-0.96 | 0-0.010     |
| Orel         | 0.02-0.86 | 0.005-0.016 |
| Samara       | 0.02-0.45 | 0.005-0.013 |
| Mokraya Sura | 0.14-0.64 | 0.030-0.160 |

One important source of nitrates and nitrites entering rivers is intensive chemicalization of agriculture based on wide use of mineral fertilizers. It has been shown<sup>12</sup> that with poor agricultural practices up to 20-40 percent of fertilizers introduced into soil wind up in the rivers. One example of

water contamination by nitrogen-containing compounds is the Zdvizh River, which flows through a region of intensive agricultural production. The nitrate concentration in this river due to leaching of fertilizer residues reached 7.3 mg N/liter. We found noticeable concentrations of nitrite nitrogen in the Irpen River, which also drains an area of intensive farming.

Livestock complexes are another important source of accumulation of nitrate nitrogen in rivers<sup>3</sup>. Many of them were built near rivers or near the tributaries of the principal rivers serving as sources of centralized industrial and drinking water supply. The concentration of  $\text{NH}_3$  in animal husbandry wastes may reach hundreds and thousands of milligrams per liter.

Liquid industrial, municipal and domestic wastes have great significance to contamination of river water. The quantity of nitrogen in domestic wastes is approximately 5 kg per person per year<sup>2</sup>. A typical example of such contamination is the Lybid River. The concentration of nitrite nitrogen in it reached 0.3 mg N/liter, and the nitrate concentration attained 2.96 mg N/liter. Surface runoff from the territory of Kiev apparently has an important place in the total flow of nitrogen compounds into this river. It has been calculated for example that up to 0.36 mg/liter nitrite nitrogen can enter together with melt water from cities<sup>13</sup>.

High concentrations of nitrite nitrogen (0.16 mg N/liter) in the Mokraya Sura River are also the consequence of its contamination associated with human activity: It is the recipient of water from Dnepropetrovsk's treatment plants.

Phytoplankton development in the Dniepr's tributaries has a certain influence on the concentration of nitrates and nitrites in them: Vital activities of phytoplankton cause the compounds in question to decrease in concentration. However, in comparison with reservoirs, intensive development of algae does not occur in rivers (biomass did not exceed 12 mg/liter during the time of the research). Therefore the nitrate and nitrite concentrations remain rather noticeable in them even in the warm part of the year.

In winter the concentration of nitrate and nitrite nitrogen in rivers is the highest, which is explained chiefly by attenuation of biological processes (weak development of phytoplankton, absence of vegetating higher aquatic plants etc.)

Excess quantities of soil nitrates may affect man through the water of local sources—wells. The increase in the nitrate load on man is known to be directly proportional to the magnitude of nitrate contamination of water sources<sup>11</sup>. Our research on the actual levels of nitrate accumulation in wells of Kiev and Cherkassy oblasts, UkrSSR showed that the concentration of these compounds exceeds the maximum permissible concentration (10 mg N/liter) in most of them. The nitrate concentration in drinking water from wells in Kiev Oblast was within 10.8-168 mg N/liter. Nitrate concentrations from 0.78 to 113.3 mg N/liter are typical of wells in Cherkassy Oblast.

Wells located near mineral fertilizer storage sites deserve special attention. The nitrite concentration in some of them (Kiev Oblast) was 0.450-1.33 mg N/liter, and the nitrate concentration was 68-168 mg N/liter.

The high concentration of the compounds in question in local water sources is explained chiefly by contamination of



underground water, as well as by the almost complete absence of algae in them, as a result of which they are not actively utilized.

Thus accumulation and circulation of nitrogen-containing compounds— nitrates and nitrites—in the water of different types of water basins proceed in different ways. The maximum nitrate concentrations are encountered in the upper horizons of underground water entering wells. The increase in the concentration of these substances in drinking water is most significant in zones of intensive farming, and primarily near places of open storage of mineral fertilizers. In surface water basins (reservoirs, rivers), the processes of accumulation of mineral forms of nitrogen and development of photosynthetic aquatic communities are inversely dependent. For this reason a decrease in the concentrations of nitrates and nitrites is observed in water basins during the time of intensive vegetation of algae and higher aquatic plants.

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**Complete Genome Sequence of Eastern Enquine Encephalomyelitis Virus (EEEV)**

927C0298A Moscow MOLEKULARNAYA GENETIKA, MIKROBIOLOGIYA I VIRUSOLOGIYA in Russian No 5, May 91 (manuscript received 02 Jul 90) pp 8-15

[Article by V.Ye. Volchkov, V.A. Volchkova and S.V. Netesov, "Vektor" Scientific Industrial Association, All-Union Scientific Research Institute of Molecular Biology, Ministry of Medical Industry, Koltsovo, Novosibirsk Oblast; UDC 576.833.26:[578.52:577.212.3]

[Abstract] Conventional techniques of genetic engineering and nucleotide sequencing were employed for determination of the complete sequence of the EEEV. The efforts involved preparation of a cDNA copy of the 42S RNA genome, incorporation into a plasmid, and amplification in *E. coli*. In addition, comparative studies were conducted on the derived amino acid sequences of proteins E1, E2 and E3 encoded by 26S mRNA of different EEEV strains. The compilation of the sequence database represents the initial stages in construction of engineered vaccines against EEEV and other alphaviruses. Figures 4; tables 1; references 30: 2 Russian, 28 Western.

**Transposon-Based Studies on Genetics of *Vibrio Cholerae* Non-O1**

927C0298B Moscow MOLEKULARNAYA GENETIKA, MIKROBIOLOGIYA I VIRUSOLOGIYA in Russian No 5, May 91 (manuscript received 14 Jun 90) pp 15-19

[Article by Ye.A. Zhuravleva and N.I. Smirnova, "Mikrob" All-Union Scientific Research Antiplague Institute, Saratov; UDC 579.843.1:579.252.2]

[Abstract] Chromosome mapping was performed on *V. cholerae* non-O1 by the introduction of a series of transposons into the chromosome via plasmid vectors and subsequent isolation of plasmid-free clones. Highest stability was seen in the case of Tn5-Mob (98-100 percent) and Tn601 (100 percent), while Tn9 and Tn10 loss was in the 64-76 percent range. The frequency of induced auxotrophy

was generally high, ranging from 4 to 18 percent, with most of the auxotrophs retaining specific antibiotic resistance. Analysis of more than 80 mutants led to identification of 11 genetic linkage groups at three chromosome regions representing 28 genes encoding synthesis of growth factors. In addition, efficient donors of chromosomal markers were constructed using Tn5-Mob and helper plasmid RP-4, the latter displaying a high transfer efficiency of  $3.6 \times 10^{-2}$ . During conjugation the donors transmitted the markers in a directional manner as indicated by a transfer efficiency spectrum ranging from  $2 \times 10^{-4}$  for Trp-80,  $4.5 \times 10^{-4}$  for His-81 to  $10^{-7}$  for Ile-80. Tables 6; references 18: 8 Russian, 10 Western.

**Cloning of Human Prointerleukin-6 Encoding cDNA**

927C0298C Moscow MOLEKULARNAYA GENETIKA, MIKROBIOLOGIYA I VIRUSOLOGIYA in Russian No 5, May 91 (manuscript received 20 Jun 90) pp 19-21

[Article by S.V. Kotenko, N.V. Taranenko, V.V. Konstantinova, S.A. Ketlinskiy and Yu.P. Vinetskiy, All-Union Scientific Research Institute of Genetics, Moscow; All-Union Scientific Research Institute of Highly Purified Biological Preparations, Leningrad; UDC 612.112.94.015.2:612.6]:577.21]

[Abstract] Conventional cloning techniques and complementation probes were utilized in cloning cDNA encoding human proIL-6 from mononuclear cells of donor blood, using a cDNA library. The nucleotide sequence of proIL-6 cDNA was determined to consist of 47 nucleotides in the 5'-nontranslatable end, 639 nucleotides encoding 213 amino acid residues, and 415 nucleotides forming the nontranslatable 3'-region. Comparison with other gene banks encoding proIL-6 revealed two potential nucleotide substitution sites which, however, would not lead to amino acid substitutions. The majority of such differences reside in the 3'-nontranslatable region. Comparison with published data demonstrated that the sequenced cDNA corresponded most closely to monocyte proIL-6. Figures 1; tables 1; references 18: 2 Russian, 16 Western.

**Diagnosis of Tick-Borne Encephalitis (TBE) By Indirect Immune Rosette Formation (IIRF)**

927C0297B Moscow *ZHURNAL MIKROBIOLOGII, EPIDEMIOLOGII I IMMUNOBIOLOGII* in Russian No 5, May 91 (manuscript received 17 Apr 90) pp 33-35

[Article by L.P. Bykova, V.M. Minayeva, R.Z. Kuzyayev, I.V. Shchitsina, T.G. Parkhomenko and V.V. Shcherba, Perm Medical Institute; UDC 616.98:578.833.26]-078.333]

[Abstract] Efficiency of IIRF was assessed on 200 patients in a Perm hospital in order to improve laboratory diagnosis of TBE. The IIRF test was positive in 70.15 percent (47) of the 67 patients with TBE positive serologies and in 24.06 percent (32) of the 133 who were serologically negative. The respective indices of IIRF in these two groups were 5.97 and 2.76 percent. In the serologically positive cohort IIRF was positive in 77.41 percent of the patients with the meningeal form of TBE, 63.63 percent of febrile cases, and in both of the two focal cases. In addition, IIRF was shown to be some 12 percent more sensitive than passive hemagglutination and, accordingly, shown to be a useful diagnostic modality for early diagnosis of TBE. Tables 4; references 7: Russian.

**Detection of IgM by Enzyme Immunoassay (EIA) and Passive Hemagglutination (PH) in Diagnosis of Tick-Borne Encephalitis (TBE)**

927C0297D Moscow *ZHURNAL MIKROBIOLOGII, EPIDEMIOLOGII I IMMUNOBIOLOGII* in Russian No 5, May 91 (manuscript received 05 Sep 90) pp 77

[Article by Ye.V. Kudrevatykh, R.Z. Kuzyayev, V.M. Minayeva, L.K. Yaroshenko and Ye.N. Volynkina, Perm Oblast Epidemiologic Station; UDC 616.831-002-033.7:578.833.26]-022.39-078.338]

[Abstract] Trials were conducted on the applicability of EIA and PH in the early diagnosis of TBE in comparison with the conventional passive hemagglutination inhibition (PHI) tests. Studies with 1734 serum samples obtained from 779 patients with TBE in Perm showed excellent correlation between the results obtained with EIA and PH. However, in 11-16 percent of the cases EIA and PH failed to detect IgM antibodies detected by PHI. Studies on early sera showed that within six days of onset of TBE EIA was positive for IgM antibodies in 67 percent of the cases and PH in 85.6 percent. The level of detection rose to 88-92 percent by both methods after 7-14 days, and to 94 percent after 15-23 days.

**Opioid Binding Immunoglobulins in Atopic Dermatitis and Drug Addiction**

927C0319A Moscow *IMMUNOLOGIYA* in Russian No 2, Feb 91 (manuscript received 23 Jun 90) pp 42-44

[Article by O.Yu. Polevaya, V.A. Samsonov, M.A. Myagkova, M.V. Lushnikova and I.G. Yashayeva, Institute of

Physiologically Active Substances, USSR Academy of Sciences, Chernogolovka; TsKVI [expansion unknown], USSR Ministry of Health, Moscow; UDC 616.5-002-056.3+616.89-008.441.33]-07:616.153.962.4-097-078.3]

[Abstract] A comparative study was conducted on neuroimmunological status of 16 patients with atopic dermatitis, 17 drug addicts and 10 control subjects. The selected approach involved ELISA assessment of anti-endogenous opioid levels of IgM. Analysis of the serum samples revealed a pattern of somewhat depressed IgM levels in patients with atopic dermatitis and elevated levels in drug addicts vis-a-vis control samples. However, in the drug addicts IgM was significantly elevated only against dermorphin and its synthetic analog U<sub>1</sub>. In the atopic dermatitis group significant depression of IgM antibodies was noted against  $\beta$ -endorphin, leu-enkephalin, met-enkephalin and dermorphin. These observations demonstrate that an imbalance of neuroimmunologic factors occurs in these conditions. In addition, it appears that determination of specific IgM antibodies may have diagnostic value in atopic dermatitis. Figures 1; tables 2; references 15: 8 Russian, 7 Western.

**Indicators of Nonspecific Resistance in HIV Infections**

927C0319B Moscow *IMMUNOLOGIYA* in Russian No 2, Feb 91 (manuscript received 15 Apr 90) pp 12-14

[Article by A.G. Rakhmanova, V.A. Isakov, A.Yu. Kolmakov, N.V. Badosova, T.P. Demidenko and V.S. Omelchenko, Leningrad Institute of Advanced Training for Physicians imeni S.M. Kirov, USSR Ministry of Health; UDC 616.98:578.826.6]-092.612.017.1.064]-07]

[Abstract] Comprehensive immune assessment studies were performed on 32 Soviet and foreign nationals in various stages of HIV infection diagnosed in Leningrad since 1987. The clinical findings and laboratory reports were those typical of this condition, and involved significant elevations of IgA, IgA and IgM in patients with HIV infections, AIDS-related complex (ARC), and cases with persistent generalized lymphadenopathy. However, IgD concentration was markedly depressed in the initial stages of HIV infection, while those cases that had advanced to the ARC stage also presented with significant depression of transferrin and of the C3 component of the complement system. Cellular immunity was also depressed, as evident in reduction of E-rosette forming cells and theophyllin resistant rosette formers. Theophyllin-sensitive cells were not affected, resulting in a reduction of the rosette-forming theophyllin resistant/sensitive cell ratio to 1.6 in ARC cases versus a control value of 3.0. Cytotoxicity tests with monoclonal antibodies also demonstrated depression of the OCT4/OCT8 cells in the ARC patients. Tables 2; references 15: 8 Russian, 7 Western.

### Immunoadsorption Therapy for AIDS

927C0297A Moscow *ZHURNAL MIKROBIOLOGII, EPIDEMIOLOGII I IMMUNOBIOLOGII* in Russian  
No 5, May 91 (manuscript received 13 Jun 90) pp 24-27

[Article by B.A. Shmatkov and D.V. Kulayev, Scientific Research Institute of Physicochemical Medicine, RSFSR Ministry of Health, Moscow; UDC 616.098]:027.078]

[Abstract] Theoretical studies were conducted on the application of hemoperfusion over immunoadsorbent beds as a therapeutic modality in AIDS. The kinetic considerations demonstrated that immunoadsorption will not benefit patients in the early stages of AIDS. In such cases gp120, an important pathogenetic molecule, is completely bound to cellular  $CL_4$  receptors with a binding constant that is some three-fold greater than the affinity that can be expected for extracorporeally employed immunoadsorbents. Under optimum binding and equilibrium conditions approximately 6.6 years of continuous hemoperfusion would be required for removal of half the body load of gp120. However, in advanced cases of AIDS hemoperfusion over immunoadsorbents is a feasible modality since a significant portion of gp120 is bound in immune complexes. Since the affinity constants of the immunoadsorbents exceed that characteristic of immune complexes by some two to three orders of magnitude, efficient removal of gp120 can be anticipated in the course of hemoperfusion. References 19: Western.

### Evaluation of Effectiveness of Influence of Magnetic Eddy Field on Course of Tumor Process in Generalized Cancer of the Mammary Gland

927C0328A Moscow *SOVETSKAYA MEDITSINA* in Russian No 7, Jul 91 (manuscript received 11 Jun 90) pp 25-27; UDC 618.19-006.6-085.847.8-036.8-07]

[Article by N. G. Bakhmutskiy, T. A. Pyleva, V. Ye. Frolov, D. A. Sinitskiy, and I. M. Ripa, Production/Scientific Research Laboratory for Use of Magnetic Fields in Oncology, Kuban Medical Institute, Krasnodar]

[Abstract] A good deal of data exists on the possibility of using magnetic fields to treat malignant tumors, but opinion on the mechanisms of the effects produced is varied. The researchers here evaluated the effectiveness of a technique advanced by D. A. Sinitskiy that uses an eddy magnetic field. The evaluation involved a magnetic therapy unit called a Magnitoturbotron that generates a rotating field that has an induction cycle that goes from zero to a given maximum and back to zero in two minutes. The field gradient distribution in the working chamber of the inductor is as follows: the magnitude of the vector of the magnetic induction has an identical value at any point in the cross-section of the inductor; along the axis, the absolute value of the vector is uniform for about 1000 mm and diminishes toward the ends of the working chamber. The unit affects the whole body of the patient, who is moved through the unit on a carriage during the procedure. This paper elucidates the results of a course of 30 procedures performed with the unit, with magnetic field induction reaching a maximum of 3 mT and a procedure averaging one hour. The patients were women with primary incurable tumors; recidivistic tumors; intradermal and subdermal metastases; metastases in regional and contralateral lymph nodes and in opposite mammary gland; and metastases in lungs, bone, and brain. Before the magnetic-field therapy, the patients had been

treated with various combinations of surgical procedures, radiation therapy, and chemotherapy. The researchers found dramatic or substantial improvement in 27 of 51 patients ("dramatic improvement" defined as tumor or metastases disappearing or diminishing by at least 50 percent after one month of treatment; "substantial improvement," diminution by 25-50 percent after one month). Improvements of more than 50 percent were noted in patients in whom the process was localized in the form of intradermal or subdermal metastatic nodes in the vicinity of post-op scarring and isolated metastases in regional lymph nodes. In two patients, extending the course of the procedures to beyond 30 resulted in complete regression of the tumors. References 7: 5 Russian, 2 Western.

### Use of Antioxidants in Treatment of Vibration Sickness

927C0328B Moscow *GIGIYENA TRUDA I PROFESSIONALNYYE ZABOLEVANIYA* in Russian  
No 4, Apr 91 (manuscript received 11 Apr 90) pp 18-20

[Article by V. G. Artamonova, L. V. Kuskova, Health-and-Hygiene Medical Institute, Leningrad; UDC 616-057-02:613.644]-085]

[Abstract] Stresses such as vibration result in an elevation of free-radical oxidation of lipids. From a pathophysiological standpoint, vibration sickness can be regarded as a variation of the membrane-pathological process characterized by damage to the cell membranes and intracellular organelles, accumulation of primary and secondary lipid-peroxidation products, and a lowering of the activity of the antioxidant system. The researchers here used the Bieri methods to determine vitamin E levels in blood plasma. Functional tests were used to determine those levels in the body. The researchers also employed clinical, physiological, and biochemical tests to study 101 vibration sickness patients whose work involved the use of vibrating tools for cutting and grinding. Combined treatments involving ganglioblockers, central cholinolytics, vascular dilators, sedatives, and vitamins for 20 days resulted in the elimination or reduction of pain and paresthesia in the hands, depending of the stage of the illness. The inclusion of vitamin E in the form of  $\alpha$ -tocopherol in the combined treatments is considered necessary for proper results, as it improved the redox processes at the level of the biological membrane. References 7: 3 Russian, 4 Western.

### Acute Occupational Poisoning in Closed Spaces

927C0328C Moscow *GIGIYENA TRUDA I PROFESSIONALNYYE ZABOLEVANIYA* in Russian  
No 4, Apr 91 (manuscript received 11 Jun 90) pp 22-24

[Article by V. A. Meleshchenko, V. A. Mikhayev, City Health-Epidemiological Station, Moscow; UDC 613.632.4-074]

[Abstract] One of the most complex tasks of the health station physician is the investigation of occupational poisonings. He often finds health regulations to be inadequate or completely lacking and rules that are violated and, sometimes, obstruction of the investigation by authorities who do not wish to explain what happened and why it happened. In 1986-1989, a total of 18 individuals died while working in closed spaces, with most of them welding water mains or sewerage systems. To prevent such accidents, the researchers suggest a country-wide regulation that includes a list of safety measures to be taken during construction and work done in closed spaces and techniques for laboratory/instrument monitoring. The regulation would specify that, before any work is done in the closed space, the proper ventilation must be provided; the type of ventilation would be specified. References 4: Russian.



### Effect of Industrial Air Pollution on Soil Microbiology

927C0285C Kiev *MIKROBIOLOGICHESKIY ZHURNAL in Russian* Vol 53 No 6, Nov-Dec 91 (manuscript received 21 Feb 91) pp 27-34

[Article by V.P. Stefurak, Ivano-Frankovsk Medical Institute; UDC 631.46.1]

[Abstract] Status of soil microbiology in the vicinity of a magnesium plant in Kalush, Western Ukraine, was monitored to assess the impact of industrial air pollution. Samples of derno-podzolic obtained in 1984-1987 at distances ranging from 500 m from the plant to 25,000 m showed significant alterations in the microbial ecology. In general, the bacteriologic studies revealed a greater than four- to five-fold increase in oligotrophic microorganisms, while nitrogen-fixing, nitrifying and cellulose-degrading microorganisms diminished significantly. The changes also included a 21 percent increase in the isolation of sporogenic microbes. These observations indicate that changes in the microbial flora may be utilized as bioindicators of soil pollution. Figures 1; tables 3; references 17; Russian.

### Comparative Assessment of Serologic Diagnosis of Epidemic Typhus

927C0297C Moscow *ZHURNAL MIKROBIOLOGII, EPIDEMIOLOGII I IMMUNOBIOLOGII in Russian* No 5, May 91 (manuscript received 12 Feb 90; in final form 08 Sep 90) pp 47-50

[Article by Yu.A. Nedyalkov, E.I. Drobyshvskaya, M.M. Dodonov, N.F. Fetisova, V.G. Nesterenko and I.V. Tarasevich, All-Union Scientific Research Institute of Epidemiology and Microbiology imenin N.F. Gamaleya, USSR Academy of Medical Sciences, Moscow; UDC 616.098:027.078]

[Abstract] Comparative assessment was conducted on serologic methods of diagnosis of epidemic typhus using seven sera from patients and 377 serum samples obtained in an endemic area in Moldova. Sera from the patients gave positive reactions with *R. prowazekii* antigens in indirect immunoenzyme assay (IEA), capture ELISA (CE), indirect immunofluorescence (IF) and in immunoblotting with the species-specific 80-120 KD proteins. In addition, analysis of sera from the endemic area showed that 22.5 percent (85) were positive in IF, 25.5 percent (96) in IEA and 1.6 percent (6) in CE. In general, CE and IEA were found to have equivalent sensitivity but differed markedly in specificity. The greater specificity of CE was attributed to the use of monoclonal antibodies, suggesting that CE may be suitable for early ( $\mu$ -CE) and retrospective ( $\gamma$ -CE) diagnosis of epidemic typhus. Figures 2; tables 1; references 15: 5 Russian, 10 Western.

### Conjugative Transfer of Sa Plasmid Via Recombinant pSKFT5 Plasmid From *Escherichia Coli* to *Francisella Tularensis*

927C0315A Moscow *MOLEKULARNAYA GENETIKA, MIKROBIOLOGIYA I VIRUSOLOGIYA in Russian* No 5, Aug 91 (manuscript received 11 Jun 90) pp 13-16

[Article by A.P. Pomerantsev, I.V. Domaradskiy and N.A. Shishkova, All-Union Scientific Research Institute of Applied microbiology, Obolensk, Moscow Obl.; UDC 579.841.95:579.254.2]

[Abstract] Transfer of Sa plasmid (IncW incompatibility group) from *E. coli* HB101 donors to *F. tularensis* 15, a vaccine strain, via conjugation was attained with recombinant pSKFT5 plasmid bearing Sa sequence. pSKFT5, a deletion mutant of pSKFT bearing a fragment of the tularemia chromosome, arose as a consequence of recombinational events in *E. coli* bearing both Sa and pSKFT. The *F. tularensis* recipients acquired the Cm<sup>R</sup> phenotype with a frequency of 10E-7. Since transfer was successful only with pSKFT5, it appears that pSKFT5 encodes a function that is mandatory for Sa transfer. It may be that pSKFT5 encodes a *F. tularensis* gene responsible for aggregation of donor and recipient cells which renders interspecies conjugation efficient. Subcloning of the *F. tularensis* fragment in pSKFT5 demonstrated that the size of this fragment is ca. 1 kpb. Reverse transfer of Sa from *F. tularensis* to *E. coli* donors proceeds with a frequency of 10E-8. Figures 3; references 24: 4 Russian, 20 Western.

### Protein Expression in Long-Term in Vivo Culture of *Yersinia Pestis*

927C0315B Moscow *MOLEKULARNAYA GENETIKA, MIKROBIOLOGIYA I VIRUSOLOGIYA in Russian* No 5, Aug 91 (manuscript received 20 Dec 90) pp 16-20

[Article by G.Yu. Kulyash, Ye.M. Golovko and M.N. Lyapin, "Mikrob" All-Union Scientific Research Antiplague Institute, Saratov; UDC 579.842.23:[579.222:547.96].083]

[Abstract] Simulation of the impact of in vivo conditions on the metabolic status of *Y. pestis* EV was modeled by long-term cultivation of the cells in semipermeable chambers implanted in the peritoneal cavity of guinea pigs as described by Day, et al. [*J. Infect.*, 2:39, 1980]. In vivo culture of *Y. pestis* for 90 days did not induce any significant phenotypic differences in comparison with cells grown at 37° on Hottinger's medium. However, beginning with day five and persisting for the duration, SDS-polyacrylamide gel electrophoresis demonstrated changes in the protein spectrum. These consisted of the disappearance of a few bands which reappeared on in vitro culture. In addition, after 30 days of in vivo culture new protein bands appeared which were not evident in in vitro cultures, and certain bands—particularly those below the 45 KD marker—stained darker than in in vitro cultures. The protein patterns subject to change involved the species-specific fraction I antigens. Figures 2; references 20: 9 Russian, 11 Western.

### Seventh Cholera Pandemic in the World and USSR

927C0347A Moscow *ZHURNAL MIKROBIOLOGII, EPIDEMIOLOGII I IMMUNOBIOLOGII in Russian* No 6, Jun 91 (manuscript received 26 Sep 90) pp 37-40

[Article by M. I. Narkevich, G. G. Onishchenko, Yu. M. Lomov, E. A. Moskvitina, L. S. Podosinnikova, G. M. Medinskiy, and A. A. Kyuregyan, Main Epidemiological Administration of USSR Ministry of Health, and Rostov-on-Don Scientific Research Plague-Control Institute, under the rubric: "Epidemiology. 1961"; UDC 616.932-036.2(100)]



[Text] The seventh pandemic of cholera began in 1961. According to WHO data, 1,713,057 cases of cholera were recorded in 117 countries on virtually all continents between 1961 and 1989. The worldwide incidence of cholera was referable mainly to Asian and African nations, where the number of patients in the pandemic constituted

1,265,906 and 473,659, respectively. Epidemics and outbreaks were recorded in countries of Europe, America, Australia and Oceania (Table 1). The data submitted here do not reflect the true extent of the cholera pandemic, since not all information by far is received by WHO, let alone data pertaining only to patients.

Table 1. Incidence of cholera over the world during the seventh pandemic, 1961-1989

| Year   | Number of cholera cases |         |                       |         |        | world total |
|--------|-------------------------|---------|-----------------------|---------|--------|-------------|
|        | Asia                    | Africa  | Australia and Oceania | America | Europe |             |
| 1961   | 61,456                  | —       | —                     | —       | —      | 61,456      |
| 1962   | 41,575                  | —       | —                     | —       | —      | 41,575      |
| 1963   | 65,357                  | —       | —                     | —       | —      | 65,357      |
| 1964   | 81,401                  | —       | —                     | —       | —      | 81,401      |
| 1965   | 51,338                  | —       | —                     | 2       | —      | 51,340      |
| 1966   | 33,779                  | —       | —                     | —       | —      | 33,779      |
| 1967   | 24,167                  | —       | —                     | —       | —      | 24,167      |
| 1968   | 27,852                  | —       | —                     | —       | —      | 27,852      |
| 1969   | 33,040                  | —       | 1                     | —       | —      | 33,041      |
| 1970   | 33,090                  | 11,195  | —                     | —       | 6      | 44,291      |
| 1971   | 97,657                  | 57,196  | —                     | —       | 95     | 154,948     |
| 1972   | 62,439                  | 6,654   | 44                    | —       | 4      | 69,141      |
| 1973   | 99,493                  | 9,193   | —                     | 1       | 302    | 108,989     |
| 1974   | 99,224                  | 6,951   | 6                     | 1       | 2483   | 108,665     |
| 1975   | 82,253                  | 6,740   | —                     | —       | 1474   | 90,467      |
| 1976   | 65,973                  | 2,791   | —                     | —       | 13     | 68,777      |
| 1977   | 50,872                  | 8,791   | 1309                  | 4       | 7      | 60,983      |
| 1978   | 50,820                  | 23,419  | 533                   | 12      | 5      | 74,789      |
| 1979   | 35,196                  | 19,634  | 51                    | 1       | 289    | 55,171      |
| 1980   | 19,505                  | 18,285  | 3                     | 13      | 16     | 37,822      |
| 1981   | 19,828                  | 17,764  | 2                     | 21      | 41     | 37,656      |
| 1982   | 15,191                  | 37,427  | 2217                  | —       | 21     | 54,856      |
| 1983   | 27,005                  | 36,722  | 319                   | 3       | 12     | 64,061      |
| 1984   | 11,801                  | 17,060  | 20                    | 1       | 11     | 28,893      |
| 1985   | 13,383                  | 27,108  | 6                     | 4       | 9      | 40,510      |
| 1986   | 5,774                   | 40,626  | 5                     | 18      | 52     | 46,473      |
| 1987   | 17,558                  | 30,929  | 1                     | 5       | 14     | 48,507      |
| 1988   | 20,872                  | 23,223  | 1                     | 10      | 14     | 44,120      |
| 1989   | 18,007                  | 35,951  | —                     | 1       | 11     | 53,970      |
| Totals | 1,265,906               | 473,659 | 4516                  | 97      | 4879   | 1,713,057   |

The epidemic process was the most intense in the world from 1967 to 1974. Then there was a decline up to 1985, and for the last four years the morbidity level became stabilized at a high level. WHO reports 44,000-52,000 cases of cholera in 26-36 countries.

In 1971-1974, peak morbidity in the world was found in countries of South-East Asia, where 70-72 percent of all cholera cases were recorded up to 1979. From 1980 on, there was a dramatic rise in share of patients in Africa (up to 62 percent).

In several countries of Asia and Africa, new and persistent endemic sites of cholera appeared (Asia: India, Indonesia, Malaysia, Singapore, Thailand; Africa: Liberia, Nigeria, Angola, Zaire, Cameroun, Tanzania), and major epidemics continue to be recorded.

In European countries, there were outbreaks of cholera in 1971-1975 in Spain (22 cases), Italy (288 cases) and Portugal (3545 cases), the infection being carried to England, France, FRG and a number of other countries where it did not cause epidemic complications.

At the same time, the infection has become ingrained in the United States, where only 37 cases of cholera were registered in the last five years<sup>8</sup>.

Analysis of worldwide morbidity revealed that, between 1965 and 1969, a total of 24 countries, mainly in Asia, reported 419,968 cholera cases; there were reports of 706,261 cases between 1970 and 1977 in 73 countries (27 in Asia, 32 in Africa, 12 in Europe, 2 in America), and from 1978 to 1989 83 countries (32 in Asia, 35 in Africa, 14 in Europe, 2 in America) recorded 586,828 cases of cholera.

The cholera situation remains poor in the world, and this is consistent with the negative prognosis of WHO<sup>10</sup>.

The main routes of dissemination of infection in the case of major outbreaks are water (Asian and African countries) and alimentary, related primarily to consumption of products of

the sea (Spain, 1971; Italy, 1973; Portugal, 1971, 1974, 1975; USA, 1988, 1989)<sup>10, 11, 14</sup>. In addition, the household route of transmission plays a significant role (Comores Archipelago, 1976; India, 1982; Central Africa, 1983, 1984)<sup>12, 13</sup>. We should note among the epidemiological distinctions of the seventh pandemic that it has lasted longer than the six preceding ones (29 years). The pandemic was caused by *Vibrio cholerae* (El Tor)<sup>2</sup>. However, outbreaks of classical cholera were recorded in Bangladesh in 1981, 1983, and 1988<sup>9</sup>. An unusually large number of countries was involved due to the intensified migratory processes<sup>7</sup>.

During the period of the seventh pandemic, 10,723 cholera cases and vibrio carriers were recorded in the USSR in 11 Union republics, with the exception of Latvia, Lithuania, Estonia and Armenia (Table 2).

Table 2. Data on cholera in 1965-1989 in different republics of USSR

| Indicator   | Number of cases in different republics |               |           |            |             |           |            |              |                |             |                 |
|---|--|---------------|-----------|------------|-------------|-----------|------------|--------------|----------------|-------------|-----------------|
|   | RSFSR                                  | Ukrainian SSR | Uzbek SSR | Kazakh SSR | Turkmen SSR | Tajik SSR | Kyrgyz SSR | Georgian SSR | Azerbaijan SSR | Moldova SSR | Belorussian SSR |
| Number of patients and vibrio carriers (absolute) | 7720                                   | 1337          | 820       | 192        | 170         | 56        | 7          | 73           | 253            | 72          | 23              |
| Share (percentage)                                | 72.0                                   | 12.5          | 7.5       | 1.8        | 1.6         | 0.5       | 0.06       | 0.7          | 2.4            | 0.7         | 0.2             |

The epidemic manifestations of cholera in our country can be divided into three periods: I—1965-1969; II—1970-1977; III—1978-1989.

The first cholera outbreak in the USSR was recorded in 1965 in Kara-Kalpak ASSR and Khorezm Oblast of Uzbekistan.

The beginning of the pandemic in the USSR was preceded by activation of this process in the world in 1964, when major epidemics struck several Asian countries, including some bordering on ours. It is common knowledge that the Uzbekistan epidemic was related to importation of the infection, in particular from Afghanistan<sup>1</sup>.

In subsequent years, there were local outbreaks and isolated cases of cholera in Uzbekistan (1968), Turkmenia (1969), RSFSR (Dagestan, Rostov Oblast, 1969). In this period, a few strains of *V. cholerae* were isolated, mainly from superficial bodies of water in the territories mentioned, as well as in Azerbaijan and Krasnodar Kray, i.e., the range of the infection began to expand.

The years of 1970-1977 were a period of intense spread of cholera, when epidemic complications were recorded in more than 80 administrative regions of the nation.

Cholera cases peaked in 1970, when there was a total of 3989 victims and vibrio carriers, due to another case of bringing infection to Odessa, Kerch, Astrakhan<sup>4, 6</sup> and Batumi via maritime transport, followed by migration of infection from the primary sites in the same year to 38 cities of the land, in spite of the set of cholera-control measures that were implemented.

There were other instances of bringing the infection in from other countries: to Azerbaijan from India, Jordan and Iran (1970-1972), and to Kemerovo Oblast from Egypt (1975).

It must be noted that there was progressive spread of cholera over our country, as is inherent in pandemics. Major outbreaks were observed in 1970-1971 in the Volga region (Astrakhan, Volgograd, Saratov, Kuybyshev and Ulyanovsk oblasts)—5584 victims and carriers, in the Ukraine (Odessa, Crimea and other oblasts)—785, Georgia—53, Azerbaijan—42, Tajikistan—41 victims and carriers.

In subsequent years, cholera spread to new regions causing outbreaks in Northern Caucasus (Rostov Oblast, Stavropol and Krasnodar krais, and Dagestan ASSR)—1090 victims and vibrio carriers, in the Volga-Vyatka river region (Kirov, Gorkiy oblasts, Bashkir ASSR)—594, and West Siberia (Novosibirsk Oblast, Omsk, Barnaul)—226 victims and carriers.

The morbidity indicators fluctuated in our country from 0.8 (1970) to 0.001 (1977) per 100,000 population.

The intensity of the epidemic process was related to the route of transmission.

The largest number of cholera outbreaks in the 1970's occurred in Astrakhan Oblast (1970-1973), Kerch, Batumi, Odessa, Volgograd (1970-1972), Omsk (1972), Rostov Oblast (1973-1975), Novosibirsk, Barnaul (1973), Dagestan ASSR (1973), Mariupol, Kirov (1974), Odessa Oblast (1977) and other regions was related primarily to transmission via the water route (recreational activities in the water, use for household and drinking purposes of water from

superficial reservoirs, into which inadequately treated and decontaminated liquid sewage was usually dumped).

It should be noted that virulent toxigenic strains of *V. cholerae* were isolated from virtually everyone and from bodies of water in the 1960's and 1970's when there were epidemic complications with transmission via the water route<sup>3</sup>.

Major cholera outbreaks via the alimentary route were caused by *V. cholerae* contamination of dairy products (Donetsk, Donetsk and Kherson oblasts, 1971-1972) and seafood (Kerch, 1970)<sup>4</sup>. The alimentary route of transmission was and still is one of the principal ones in onset of cholera in the Caucasus (Dagestan, 1970, 1973) and Trans-Caucasus (Azerbaijan, 1977). Both cases of the disease caused by virulent toxigenic strains of *V. cholerae*, and outbreaks of the carrier state were recorded, the latter related to avirulent, nontoxic strains.

The number of victims and carriers has been declining since 1977, and the intensity of the epidemic process has shown a tendency toward diminishing. Some local outbreaks of cholera have been reported in some regions (Uzbekistan, 1982; Azerbaijan, 1985, 1989; Ukraine, 1986; RSFSR, 1981, 1990).

In the 1976-1989 period, circulation of *V. cholerae* was recorded in 134 administrative territories of 13 Union republics<sup>3</sup>. Virulent and toxigenic strains of *V. cholerae* were found only in a few parts of Uzbekistan, RSFSR, the Ukraine, Kazakhstan, and Turkmenia, and their share dropped from 48.9-74.5 percent in the 1970's to 4.0-0.8 percent in 1984-1989.

In the absence of cholera cases in most regions, this is indicative of circulation of the pathogen among undetected carriers or victims of mild forms of cholera.

The infection did not spread when it was brought from abroad into Moscow, Leningrad and Sochi during this period (1987).

In 1990, cases of cholera were recorded in Stavropol and Rostov Oblast. Cholera was brought to Stavropol by a group of specialists from, Syria, as confirmed by the results of bacteriological and serological tests. Infection of 49 patients with cholera and 20 vibrio carriers was related to consumption of water from a spring into which sewage contaminated with *V. cholerae* had penetrated via a subterranean level.

When the infection was carried out of the Stavropol site to Perm (three cases of cholera), Moscow (one case), Altay Krai (five cases), Krasnodar (two cases) and Volgograd (one case), no epidemic complications were caused due to prompt implementation of cholera-control measures.

In the Azovskiy Rayon of Rostov Oblast there was a local outbreak, during which five cholera victims and four vibrio carriers were detected. The infection occurred from using for household and drinking purposes water from the Don River downstream from the dumping of rather large amounts of untreated sewage from households.

Analysis of the rate of development of the epidemic cholera process in the USSR and in the world, as related to the start of pandemic spread of the disease (1965 and 1961, respectively), it was established that it declined in the USSR and rose virtually annually in the world (with the exception of

1967, 1969 and 1984). However, the situation regarding cholera in our country as a whole can be considered unstable.

The foregoing, as well as the continuing intensive contamination of environmental objects, compel us to believe that the prognosis is poor for cholera in different parts of our country. For this reason, there is increased importance of epidemiological surveillance of cholera and refinement of cholera-control tactics.

#### Conclusions

1. The seventh cholera pandemic continues. It has lasted longer than the six preceding ones and involves a large number of countries on all continents.
2. The epidemic manifestations of cholera in our country during the seventh mic caused major outbreaks in 1965 and 1970-1974 because the infection was brought in from abroad, and this was followed by a decline in morbidity, reports of sporadic cases of cholera, and extensive circulation in the environment of primarily avirulent and nontoxic strains of *V. cholerae*.
3. Annual records of cholera cases and detection of virulent and toxigenic strains of *V. cholerae* in superficial bodies of water of some regions are indicative of an epidemically unstable situation regarding cholera.

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### **Cholera-Control Measures Implemented in the USSR During Seventh Cholera Pandemic**

927C0347B Moscow ZHURNAL MIKROBIOLOGII, EPIDEMIOLOGII I IMMUNOBIOLOGII in Russian No 6, Jun 91 (manuscript received 13 Nov 90) pp 40-43

[Article by M. I. Narkevich, G. G. Onishchenko, Yu. M. Lomov, A. A. Kyuregyan, G. M. Medinskiy, and E. A. Moskvitina, Main Epidemiological Administration of USSR Ministry of Health, and Rostov-on-Don Scientific Research Plague-Control Institute; UDC 616.932-084.4.47+57]

[Text] In the 1960's and 1970's, after the seventh cholera pandemic reached the USSR, scientific research, particularly dealing with epidemiology of this infection, usually lacked integrity in the study of the problem, did not take into consideration the specific effect of social, ecological and other factors on the epidemic process. As a result, the efficacy of preventive and epidemic-control measures was not always correctly assessed, while recommendations on their content, scope and tactics were not adequately argued, they were prepared without consideration of the specific epidemic situation and aggregate of local conditions, as well as adequacy of economic expenditures and efficacy.

Already in the early 1970's, it was necessary to provide scientific validation of cholera-control measures with consideration of the epidemiological distinctions of El Tor cholera and nature of the epidemic process in different climate-geographic, socioeconomic, and sanitary-hygienic conditions. As a result, there was either total discontinuation or considerable reduction in scope of some epidemiologically insufficiently validated, ineffective and expensive steps.

For example, in 1965, during the cholera epidemic in Afghanistan, the Soviet-Afghan border was temporarily closed, which led to considerable economic detriment.

Of course, modern, rapid transport and the constantly increasing migration processes make it possible to rapidly bring cholera into any administrative territory. However, the sanitary-quarantine measures, which were implemented in our country and aimed at preventing the importation of cholera from affected countries or its spread from appearing sites, were not epidemiologically validated in some parts of the USSR, not to mention the considerable material losses. We are referring to the bans prevailing in 1965-1970 on export of foodstuffs and import of food parcels in Kara-Kalpak ASSR and Khorezm Oblast of Uzbek SSR, and certain other administrative regions.

Up to 1974, much attention was devoted to bacteriological screening of new arrivals from areas with a cholera problem, and keeping them under medical observation. For example, 19,041 Soviet citizens arrived from countries with a cholera

problem in 1970-1974, of whom 18,289 underwent bacteriological testing for cholera, while 18,826 were subject to medical observation. As a result, 14 people (0.07 percent) were found to have intestinal dysfunction without a single case of cholera.

During the same years, 722,781 foreigners arrived from countries with a cholera problem, 13,228 of whom were under medical observation, while 2765 had undergone bacteriological screening. Intestinal dysfunction was found in 156 cases (1.2 percent), but cholera or vibrio carriers was not found in any of them.

The subsequent experience gained by Soviet health care indicates that the epidemiological efficacy of sanitary and preventive measures regarding cholera, particularly, at the borders of the USSR, is far from adequate, considering the expense and labor they involved. For example, 55,003 transport units and 2,423,608 people from nearly 200 countries, including some with a cholera problem, and across the border with the Ukraine Moldova and Leningrad Oblast in 1979 arrived in Moscow alone (by aircraft). Sanitary-quarantine inspections were performed on 62 percent of the transport units and 66.6 percent of the passengers. A total of 69,997 of the new arrivals were under medical observation, and of this number, among those who sought medical attention a few were found to have enteritis, but not a single case of cholera or vibrio carrier was found. Furthermore, for only the sanitary and epidemiological station of Moscow, expenses related to relaying notifications to local health agencies concerning medical observation of individuals arriving from abroad amounted to more than 57,000 rubles in 1978 and over 44,000 rubles in 1979, according to incomplete data <sup>4</sup>.

The oldest measure for control of a cholera epidemic is quarantine. Quarantine steps were used to prevent importation of cholera to Russia as far back as 1829. They were subsequently refined, but were not effective due to the insufficient knowledge about cholera in the nineteenth century.

During the sixth pandemic (1908-1926), in essence quarantine was not used in European countries, including ours. When cholera broke out in Uzbekistan in 1965 and in Odessa, Kerch, Astrakhan, Makhachkala, Novorossiysk and a few other regions in 1970, health agencies were faced with the question of quarantine and observation as steps to localize infection sites. In a number of instances, there were absolutely no epidemiological indications for imposing a quarantine or idea about its extent. For example, a quarantine was imposed on Bukhara in 1965 because of an isolated case of cholera. Imposition of quarantines in Novorossiysk and Makhachkala in 1970 cannot be considered justified either, since there was no broad spread of cholera in these cities, and it was limited to 13 and 12 cases, respectively.

Four SKP-SKO [disease control stations and departments or battalions] manned by 161 medical workers were set up in Novorossiysk to implement quarantine measures; the barricaded region was 80 km in length, there being 700 people and 34 motor vehicles to cordon off and patrol the quarantined zone. In Makhachkala, 15 SKP-SKO were set up, with 1359 people and 44 vehicles cordoning off the quarantine zone for 142 km.

In addition to the enormous expenses for such quarantine measures and diversion of medical workers from their primary jobs, imposition of quarantine had an adverse effect on the economy of the regions involved and led to other material losses. For example, the port organizations of Novorossiysk had to pay more than 1.5 million rubles in fines for delayed loading and unloading operation<sup>6</sup> on Soviet and foreign vessels. In this regard, the statement of B. Cvjetanovic<sup>7</sup> to the effect that the economic detriment of cholera is considerably greater than can be suspected, since economic and health losses related to illness of people are considered much less important than the loss caused by unwise steps related to cholera outbreaks.

The cholera epidemics in Kerch and Odessa were full-blown; the disease spread rapidly throughout the cities where there was an enormous number of visiting vacationers (for example, in Odessa in the summertime, at any given time there are 400,000 to 500,000 organized and unorganized vacationers). However, even in these cities, provided the first cases of the disease are promptly detected and reliable epidemic-control steps are taken, in accordance with the epidemic situation, one can rapidly localize the outbreaks and avoid quarantine.

Observation of departing travelers is an essential part of the quarantine measures imposed on large cities or in administrative territories. For example, in Kerch, 37,524 people were put under observation and submitted to bacteriological

testing; this applied to 211,583 in Odessa, 17,622 in Makhachkala, and 2987 people in Novorossiysk. *Vibrio* carriers constituted 0.07, 0.05, 0.01 and 0 percent, respectively. These data illustrate the lack of justification for enormous efforts and means, as well as the achieved efficacy of epidemic control.

In recent years there has been a substantial change in the attitude toward quarantine measures. It became apparent that extraordinary steps to cordon off a site and place departing travelers under observation are superfluous.

It was shown that the spread of cholera can be contained without strict measures when leaving an involved site<sup>8</sup>.

In the early years of the seventh cholera pandemic, epidemic-control measures included special preventive treatment for patients in the incubation period. Mass-scale preventive treatment as a special measure was first used against cholera in Iran in 1965, and later in several other countries, including the USSR. In the opinion of N. N. Zhukov-Verezhnikov and Ye. P. Kovaleva<sup>1</sup>, special prophylaxis was of deciding importance in eradicating the cholera epidemic in Kara-Kalpak in 1965. However, thereafter, the justification for expended funds and efforts, in relation to the epidemic-control efficacy was questioned. Analysis of epidemiological efficacy of mass-scale special preventive antibiotic treatment administered in the USSR over the most critical period for cholera, from 1970 to 1974, served as grounds for this (see table).

Results of Mass-Scale Antibiotic Administration as a Special Preventive Measure at Cholera Sites

| Year          | Populated centers (administrative territories) covered on a mass scale (90 to 100 percent of the population) by special treatment | Number of infected people (sick and vibrio carriers) | Number given special treatment |            | Cases of infection among those given special preventive treatment (absolute) |                                |                | Percentage of total number of infected people |
|---------------|---|--|--------------------------------|------------|--|--------------------------------|----------------|---|
|               |   |  | absolute                       | percentage | during treatment   | within 10 days after treatment | total infected |   |
| 1970          | Odessa, Kerch, Kherson, Novorossiysk, Tajik SSR, Dagestan ASSR  | 475  | 1,363,238                      | 94.39      | 9  | 65                             | 74             | 15.60   |
| 1971          | Kerch, Donetsk, Volgograd, Donetsk Oblast   | 387  | 679,335                        | 46.34      | 2  | 90                             | 92             | 23.80   |
| 1972          | Blagoveshchensk, Shevchenko, Moscow Oblast  | 106  | 87,970                         | 94.86      | 27   | 3                              | 30             | 28.30   |
| 1973          | Rostov-on-Don, Dagestan ASSR  | 112  | 206,166                        | 22.94      | —  | 15                             | 15             | 13.39   |
| 1974          | Kerch, Kirov, Rostov-on-Don, Urzhum   | 354  | 522,374                        | 98.78      | 7  | 25                             | 32             | 9.03  |
| 5-Year totals | 15 cities and administrative territories  | 1434   | 2,859,683                      | 60.44      | 45   | 138                            | 243            | 16.95   |

The data listed in the table, which reflect only an insignificant part of relevant material for the entire country, indicate that the epidemiological efficacy of preventive antibiotic treatment is far from satisfactory. However, even these findings cannot be considered objective, since mass-scale prevention measures were combined with other preventive and epidemic-control steps. Moreover, we were impressed

by the extent of special preventive measures with respect to coverage of the public without considering the risk of infection, as well as effort and funds expended. If we consider that the cost of tetracycline for special preventive treatment is 0.76 ruble per person, for the 15 sites listed in the table a total of 2,173,359 rubles were spent, not counting the wages of medical personnel. Numerous observations



indicate that only selective special preventive treatment is effective, and it is indicated for individuals who were exposed to the same conditions as cholera victims (carriers), as well as those who came in contact with a cholera victim, either at home or someone's apartment. As noted by V. P. Sergiyev and A. S. Maramovich<sup>6</sup>, antibiotics, which elicit a brief response, cannot be a means of prevention when transmission of the pathogen via the water route persists. In the complex aggregate of measures to localize and eradicate cholera outbreaks, special preventive treatment can serve only as a strictly ancillary step<sup>2</sup>.

Mass-scale bacteriological screening for cholera was carried out after the epidemic cholera outbreaks in Uzbekistan in 1965. Detection of even isolated cases of cholera served as an indication for this, and the screening often covered everyone. Implementation of these tests required deployment of a high-power laboratory base, formation of special brigades to collect specimens, providing them with transport, creating a large stock of nutrient media and diagnostic agents, etc. For example, one-tenth of all residents of Uzbekistan were screened between 1966 and 1971, and 33 vibrio carriers were found. Within the first two to three months after eradication of cholera outbreaks, from 1970 to 1974 1,750,368 people were tested, and as a result 16 vibrio carriers were found (0.09/10,000 tested).

Thus, it was necessary to test 109,000 people to detect one vibrio carrier.

These data are indicative of the rather low efficacy of the screening. It is unlikely that the isolated vibrio carriers (particularly if we consider that the carrier state is very brief) could play any appreciable part in the spread of infection, let alone allow it to become ingrained. As for the material aspect of this measure, in the years indicated a total of 5,093,570 rubles were spent over the 13 administrative territories, not counting transportation expenses, diversion of medical personnel from their regular jobs, organizational problems, etc.

These data served as a rather weighty argument favoring discontinuation of mass-scale bacteriological screening starting in 1975. Thereafter, vibrio carriers were picked up in the course of screening different groups and individuals presenting an overt risk of infection.

Analysis of the results of bacteriological tests and clinical observations over a period of many years made it possible to shorten dispensary observation time for cholera victims and vibrio carriers from one year to three months and, accordingly, to decrease the frequency of their bacteriological testing.

We have not studied the efficacy of specific vaccination in epidemiologically controlled tests. On the basis of investigation of immunological changes resulting from vaccination, I. V. Kiseleva et al.<sup>3</sup> proved the desirability of changing from two-fold to single vaccination against cholera, which rendered it considerably cheaper and simpler.

The epidemiological efficacy was almost the same for corpuscular vaccine and cholera-anatoxin used in the USSR: the infectivity indicator (per 100,000 population) constituted 9.6 among those inoculated with cholera-anatoxin and 10.1 among those inoculated with corpuscular vaccine, whereas it was 25.2 ( $p < 0.01$ ) for the nonvaccinated population. The

coefficients of efficacy of cholera-anatoxin and corpuscular vaccine for the first three months after vaccination constituted 73.3 and 60.8 percent, respectively, and for the next three months—31.0 and 48.7 percent.

The rather low epidemiological efficacy of the vaccines used indicates that they must be improved.

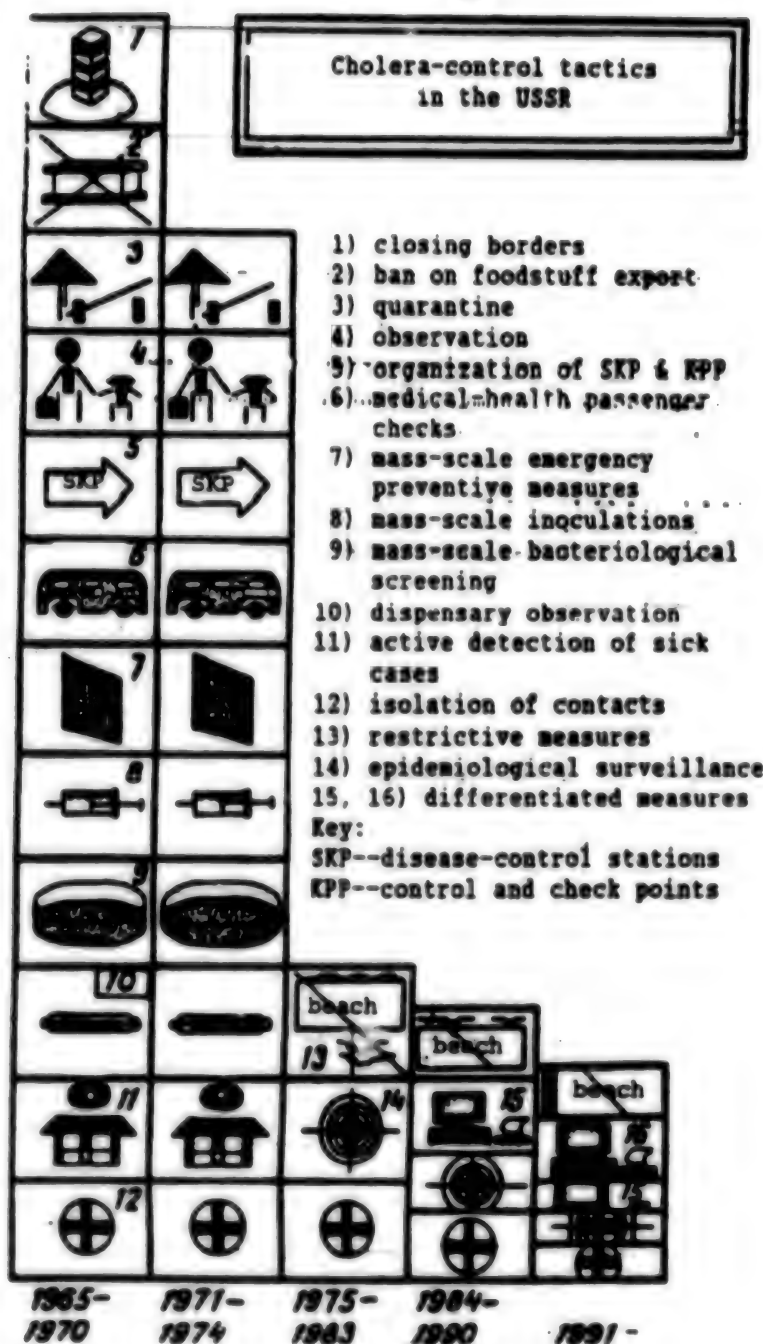
The above data indicate that the cholera-control measures implemented in the USSR since 1965 have become much simpler, sometimes they were totally discontinued and considerably reduced in cost, which had absolutely no adverse effect on the epidemiological situation with cholera. The figure graphically illustrates the changes in the main cholera-control measures from 1965 to 1990.

Improvement of cholera-control measure, and institution of epidemiological surveillance, with differentiation of their scope, led to considerable reduction of economic expenditures for eradication of outbreaks. Thus, an approximate estimate of socioeconomic expenditures for eradication of cholera constituted 36,560,603 rubles in Kara-Kalpak ASSR (1965), 56,998,072 rubles in Odessa (1970), and 484,240 rubles in Azerbaijan SSR (1989).

The experience gained in cholera-control measures made it possible to validate the efficacy of current tactics in epidemiological surveillance of cholera. Different variants have been provided for implementation of epidemiological surveillance, depending not only on specific local conditions that determine the epidemic potential, but also the properties, in particular virulence and presence of the gene for cholera toxin in cholera vibrio strains isolated from people and the environment.

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**Cloning and Detailed Mapping of Fra-Ymt Region of Plasmid pFra of Yersinia Pestis**

927C0315A Moscow MOLEKULARNAYA GENETIKA, MIKROBIOLOGIYA I VIRUSOLOGIYA in Russian No 5, Aug 91 (manuscript received 29 Nov 90; in final form 18 Jun 91) pp 19-26

[Article by P.A. Cherepanova, T.G. Mikhaylova, G.A. Karimova, N.M. Zakharova, Yu.V. Yershov and K.I. Volkovoy, All-Union Scientific Research Institute of

Applied Microbiology, USSR Ministry of Medical Industry, Obolensk; UDC 579.842.23:579.252.5].083.1]

[Abstract] Detailed mapping studies were conducted on the region of the 69 MD plasmid pFra of Yersinia pestis EV76 which encodes antigen F1 (fraction I) and Y. pestis murine toxin (Ymt). Genomic libraries were constructed using cosmid pH79 as a vector for cloning large pFra DNA fragments in E. coli HB101. The native and recombinant 1-2 MD polymeric capsular antigens isolated from Y. pestis and E. coli were shown to consist of 16 KD subunits, while

the native and recombinant 240 KD toxins had 61-63 KD subunits. The latter lacked disulfide bonding and were similar in toxicity for white mice with respective LD<sub>50</sub> values of 2.5 and 3.7 µg for the native and recombinant toxin. A nucleotide sequence corresponding to the amino acid sequence of the toxin was used to derive the sequence of the ymt gene. Figures 5; tables 1; references 31: 14 Russian, 17 Western.

**Temperate SM Phage of *Pseudomonas Aeruginosa* as Cloning Vector**

927C0316B Moscow MOLEKULARNAYA GENETIKA, MIKROBIOLOGIYA I VIRUSOLOGIYA in Russian No 5, Aug 91 (manuscript received 23 Jan 91) pp 26-29

[Article by A.M. Kulba, A.S. Gorelyshev, A.N. Yevtushenkov and Yu.K. Fomichev, Belorussian University imeni V.I. Lenin, Minsk; UDC 579.841.11:578.81:577.21]

[Abstract] Recombinant versions of the *Pseudomonas aeruginosa* temperate phage SMcst6 were constructed which bore the pectate lyase gene of *Erwinia chrysanthemi*. Transfection experiments with *Ps. aeruginosa* PAO1 as the recipient demonstrated that several recombinant SM phages functioned as efficient vehicles. One fundamental difference between the prophages of the wild-type and recombinant prophages was that the latter were less stable, an observation attributed either to deletion or inversion of a 4.8 MD HindIII fragment of the SM genome. Accordingly, the results demonstrated the vector efficiency of the SMcst6 phage despite a reduction (88 percent) or elongation (111 percent) in its DNA, depending on restriction enzymes employed. In general, the maximum size of the fragment that can be introduced into the wild-type phage and an SM-2 hybrid was shown to be 8.3 MD using HindIII and 5.1 MD using the XbaI enzyme. Figures 4; tables 1; references 14: 10 Russian, 4 Western.

**Suppression of Cellular  $\text{Na}^+/\text{H}^+$  Metabolism Inhibits Influenza Virus Activity**

927C0327A Moscow ANTIBIOTIKI I KHIMIOTERAPIYA in Russian Vol 36 No 6, Jun 91 (manuscript received 03 Apr 90) pp 35-37

[Article by V. A. Kirillov, L. N. Goreva, G. V. Vlydyko, Ye. I. Boreko, V. A. Rusyayev, and V. I. Votyakov, Belorussian Epidemiology and Microbiology Scientific Research Institute, Minsk; UDC 578.832.1:578.23]:577.352.465:576.385]

[Abstract] The relationship between inhibition of the cellular  $\text{Na}^+/\text{H}^+$  metabolism process and suppression of influenza virus (strain Rostok H7N1) activity in chick embryo fibroblasts was investigated. The antiviral properties of amiloride, ouabain, orthovanadate, and remantadine were determined in experiments on tissue cultures of primary trypsinized chick embryo fibroblasts using a screening test and plaque reduction. A 0.25 ml cell suspension ( $3.10 \cdot 10^7$  cell/ml) was incubated at 25°C for 30 minutes with a 0.25 ml solution of the preparation in a final concentration of the maximum tolerable concentration for chick embryo fibroblasts. The results demonstrated that amiloride decreased the oxidation rate in the incubation medium for  $\text{Na}^+/\text{H}^+$  metabolism by 50 percent. In addition, it was shown that the  $\text{Na,K-ATPase}$  inhibitors orthovanadate and ouabain decreased the oxidation rate in the cell medium by 40 percent. In the presence of exogenous glucose, amiloride, orthovanadate, and ouabain decreased the oxidation rate in the medium due to the diffusion of lactic acid through the plasma membrane (by 22 and 30 percent, respectively). Moreover, it was shown that remantadine, a known anti-influenza preparation, suppressed  $\text{Na}^+/\text{H}^+$  metabolism and the release of lactic acid by 60 and 67 percent, respectively, due to its membranotropic properties. The data revealed that the antiviral preparations suppressed influenza virus infection by 95 percent. The preparations were also shown to be effective against herpes simplex I, vesicular stomatitis, Venezuelan equine encephalomyelitis virus, and variolovaccine. The pathway by which the preparations probably act is as follows. The oxidation rate decreases due to an increase in the time interval necessary to decrease the intraendosomal pH to the critical level for virus propagation. The unpropagated virus enters the lysosome, where it is degraded. The utilization of the virus by the cellular lysosome prevents the development of an influenza infection in the cell. Figures 1; tables 2; references 13: 5 Russian, 8 Western.

**Multifactorial Analysis of Combined Effect of Antibiotic and Low Molecular Weight Microbial Origin Immunostimulant on Experimental Plague Infection**

927C0327B Moscow ANTIBIOTIKI I KHIMIOTERAPIYA in Russian Vol 36 No 6, Jun 91 (manuscript received 14 Nov 89) pp 41-43

[Article by A. V. Nikitin, L. N. Makarovskaya, I. P. Fomina, L. P. Ivanitskaya, G. O. Popova, N. N. Vinidchenko, Ya. N. Korganov, and M. K. Kudina, All-Union Antibiotic Research Center, Moscow; Anti-Plague Scientific Research Institute, USSR Ministry of Health, Rostov-on-the-Don; UDC 616.98:579.843.95]:092.9-085.33-036.8-07]

[Abstract] The combined effect of doxycycline and a low molecular weight microbial origin immunostimulant [not otherwise named] on an experimental plague infection was investigated in multifactorial experiments. Mongrel albino rats (18-20 g) were infected subcutaneously with the etiological agent in a dose of 100 DCL. Doxycycline was administered subcutaneously to the animals either every six hours for five days or every 24 hours for seven days in doses of 5-95 mg/kg. The immunostimulant was administered subcutaneously in doses ranging from 0.5-50 mg/kg. The results demonstrated that multifactorial analysis revealed the synergistic effect of subtherapeutic doses of doxycycline and the immunostimulant in an experimental plague infection. It was also shown that therapeutic doses of doxycycline and the immunostimulant based on survival rate indexes and survival time are more effective than the prophylactic regimen. Finally, the dose time regimens for prescribing doxycycline and the immunostimulant are optimized by means of mathematical simulation. Figures 3; tables 1; references 3: Russian.

**Salts of  $\beta$ -Glycyrrhizic Acid—Stimulators of Reparative Skin Regeneration**

927C0332A Moscow KHIMIKO-FARMATSEVTICHESKIY ZHURNAL in Russian Vol 25 No 5, May 91 (manuscript received 30 May 90) pp 39-41

[Article by V. A. Davydova, T. G. Tolstikova, L. A. Baltina, F. S. Zarudiy, Yu. I. Murinov, R. M. Kondratenko, G. A. Tolstikov, Institute of Chemistry, Bashkir Science Center, Ural Department, USSR Academy of Sciences, Ufa; UDC 615.276.017:615.243]:012.1]

[Abstract] After earlier demonstrating that derivatives of  $\beta$ -glycyrrhizic acid (I), the active ingredient of licorice extract, are highly active against inflammation, the researchers here chose to study the effect of a number of salts of  $\beta$ -glycyrrhizic acid (I) in the form of a 5 percent vaseline-based ointment on skin regeneration in rats with graft wounds and burns. The salts consisted of trisodium, sodium dipotassium, sodium dilithium, trilithium, monopotassium, tripotassium, potassium disodium, tri-O-diisopropoxyaluminum, and tri-O-methoxymagnesium, and the control preparations consisted of the Yugoslavian ointment dermazin and methyluracil, which are currently used for treating skin wounds. On day seven of treatment, all the experimental preparations had stimulated regeneration in the graft wounds to a greater extent than had the control preparations. By day 15, healing was judged to be farther along with the trisodium, sodium dipotassium, sodium dilithium, monopotassium, potassium disodium, and tripotassium salts than with controls by a factor of 25. The sodium dilithium effected complete healing by day 15. For the burns, by day seven, the experimental salts demonstrated efficacy similar to that of dermazin. By day 15, the sodium dipotassium, monopotassium, potassium disodium, and tripotassium salts promoted healing on a more effective basis than did either dermazin or methyluracil (by a factor of 1.5-4). Complete healing of burn wounds was noted on day 15 in animals treated with the tripotassium salt. Figures 1, references 5: 4 Russian, 1 Western.



**Synthesis and Antiviral Activity of 3-Cyano-2(1H)-pyridine Selenones**

927C0332B Moscow KHIMIKO-

FARMATSEVTICHESKIY ZHURNAL in Russian Vol 25 No 5, May 91 (manuscript received 27 Mar 90) pp 41-44

[Article by V. Yu. Mortikov, V. P. Litvinov, A. M. Shestopalov, Yu. A. Sharanin, Ye. E. Apenova, G. A. Gaigov, I. I. Abdullayev, T. B. Asadullayev, and F. I. Abdullayev, Institute of Organic Chemistry, USSR Academy of Sciences; Institute of Virology, USSR Academy of Medical Sciences; UDC 615.281:547.82]

[Abstract] Selenoorganic compounds are known to have a high level of antiviral activity. By the same token, many pyridine derivatives demonstrate a high degree of biological activity. Prompted by the fact that the physiological activity of selenium-containing pyridines is little studied, the researchers here combined both functions in a molecule and studied the properties of substituted 3-cyano-2(1H)-pyridine selenones in terms of their activity against influenza A virus in a culture of cells of fibroblasts of chick embryos. Compounds IX, XI, XV, XVII, and XXVII were found to have antiviral activity, with XV and XXVII most promising in the agar diffusion test. In a culture of Vero cells, XV and XVII demonstrated the highest activity against both TK<sup>+</sup> and TK<sup>-</sup> strains of herpes. Although the selenium-containing compounds demonstrated an antiviral activity that was less pronounced than that of remantadine, they were effective against RNA- and DNA-containing viruses. The researchers feel that selenium-containing compounds should be further screened for effective inhibitors of broad-spectrum viral reproduction. Figures 2, references 12: 6 Russian, 6 Western.

**Antiviral Activity of Macrocyclic Polyethers and Their Complexes With Alkaline Salts of N-Phosphorylated Amides and Thioamides**

927C0332C Moscow KHIMIKO-

FARMATSEVTICHESKIY ZHURNAL in Russian Vol 25 No 5, May 91 (manuscript received 5 April 90) pp 46-48

[Article by N. G. Zabirow, O. K. Pozdeyev, V. A. Shcherbakova, T. N. Shumilova, R. A. Cherkasov, and G. Kh. Gilmanova, Kazan State University imeni V. I. Ulyanov-Lenin; UDC 615.281:547.26:015.4.07]

[Abstract] Based on the promise held by phosphorus-containing derivatives of crown ethers in terms of antiviral activity, crown ethers were used as carriers for antiviral substances—alkaline salts of N-phosphorylated amides and thioamides—in order to attach to them an elevated penetration capacity and, consequently, to enhance their antiviral properties through direct interaction with the virus inside the cell. The compounds in the study consisted of 15-crown-5 (I), 18-crown-6 (II), benzo-15-crown-5 (III), dicyclohexyl-18-crown-6 (IV), dibenzo-18-crown-6 (V), dibenzo-24-crown-8 (VI), sodium (VII) and potassium (VIII) salts of N-diisopropoxythiophosphorylthiobenzomide, complexes of potassium salt of N-diisopropoxythiophosphorylthiobenzomide with 15-crown-5 (IX) and 18-crown-6 (X), sodium salt of N-diisopropoxythiophosphorylthiobenzomide with 18-crown-6 (XI), and potassium salt of N-diisopropoxythiophosphorylthiobenzomide with 18-crown-6 (XII). Most of the compounds studied—with the

exception of II, IV-VI—demonstrated some degree of activity against influenza virus A (H3N2). Index of protection ranged from 38 percent to 80 percent, and the survival rate of the experimental animals grew by 56.7-90 percent, as compared with control. Life span was lengthened by 0.7-25 percent. Compounds VII and VIII were found to be especially effective. Compound X exceeded VIII in antiviral activity and extended life spans by 9.2 percent. Figures 1, references 7: 6 Russian, 1 Western.

**Computer Prediction and Study of Biological Properties of Nitrofurylvinyl (Polyenyl) Quinolones**

927C0332D Moscow KHIMIKO-

FARMATSEVTICHESKIY ZHURNAL in Russian Vol 25 No 5, May 91 (manuscript received 5 Apr 90) pp 55-58

[Article by A. Rozenblit, V. Golender, N. Sukhova, and E. Lukevits, Institute of Organic Synthesis, Latvian Academy of Sciences, Riga; UDC 615.015.11:547.722.5]

[Abstract] In a search for effective biologically active substances in a number of new types of nitrofurane compounds—nitrofurylvinyl (polyenyl) quinolones—the researchers here predicted biological activity of more than 150 compounds with ORAKUL computer software. Underlying the technique they used is an algorithm based on a statistical estimate of structural traits of biological activity consisting of code descriptors. The code descriptors are made up of two potentially active centers and the links between them. The researchers assessed the probability that a compound containing a given trait would have a given level of activity—a confidence coefficient and an effectiveness coefficient, the latter showing the relationship of the first to the probability of finding a compound with a given activity via blind search. The descriptor is considered a trait of a given level of activity if both coefficients exceed certain thresholds found in learning. Learning was performed with a data bank consisting of more than 6,000 structures, plus information on their activity. The user can get not only a spectrum of predicted activities, but also all the descriptors that make up a given structure. The algorithm enables interpretation of the results and identification of substructures responsible for a given biological effect. New compounds can be synthesized with a given spectrum of activity. The mean probability of a correct prediction is 0.91 with a mean coefficient of effectiveness of the system of 2.61. The analysis performed by the researchers predicted for nitrofurylvinyl (polyenyl) quinolones with a high confidence coefficient, antitumor, antimicrobial, antihelminthic, anti-inflammatory, and antituberculosis activity for nitrofurylvinyl (polyenyl) quinolones with a high confidence coefficient. References 8: Russian.

**Effect of Certain Fluids and Steam Sterilization on Strength Properties of Polyamide Membranes**

927C0332E Moscow KHIMIKO-

FARMATSEVTICHESKIY ZHURNAL in Russian Vol 25 No 5, May 91 (manuscript received 20 Mar 90) pp 78-81

[Article by G. B. Bochkova and A. S. Yushin, Gorky Scientific Research Institute of Epidemiology and Microbiology; UDC 620.171.3:66.067.12-678.675]



[Abstract] According to the developers of the microporous capron MIFIL membranes and the FMPA polyamide filtration film, they are equal to membranes produced by Millipore, Pall, and Sartorius, which are used for sterilization of various organic solvents, dionized water, liquid pharmaceuticals and medical preparations, nutritive media, injectable solutions, blood protein preparations, and gases. In the absence in the literature of quantitative indices on the strength and deformational properties of the Soviet membranes, as well as data on the effects of their sterilization in steam, the researchers here found that, although the developers assert a high degree of elasticity for the membranes both when they are dry and when they are wet, reversibility of deformation and invariability of filtration properties are possible only when the stretching is no more than 2 percent. They did find the MIFIL and FMPA membranes to be stronger than cellulose and cellulose-based membranes and to demonstrate a lesser degree of anisotropy in terms of mechanical properties. The Soviet capron membranes, however, were not as strong as foreign-made nylon membranes and were less resistant to damage from steam sterilization. Figures 3, references 11: Russian.

#### **Synthesis and Assessment of Nitrogen-Containing Adamantane Derivatives**

927C0333A Moscow *KHIMIKO-FARMATSEVTICHESKIY ZHURNAL* in Russian Vol 25 No 7, Jul 91 (manuscript received 06 Jul 90) pp 46-49

[Article by Yu. N. Klimochkin, I. K. Moiseyev, G. V. Vladyko, L. V. Korobchenko and Ye. I. Boreko, Kuybyshev Polytechnical Institute; Belorussian SSR Scientific Research Institute of Epidemiology and Microbiology, Minsk; UDC 615.281.8:547.592.1].012.1]

[Abstract] Cursory details are presented on the synthetic rationale employed in the preparation of 17 carbamate, amide, aminoamide and aminoester congeners of adamantane as part of screening for novel antivirals. Tissue culture trials showed that 11 of the agents possessed some degree of antiviral activity against selected viruses in the following group: herpes simplex 1, vaccinia, fowl plague, RSV, VSV, VEE or ECHO-6. These observations indicate that further assessment of this class of adamantane congeners for antiviral activity is warranted. Tables 2; references 7: 5 Russian, 2 Western.

#### **Synthesis and Assessment of Sulfur-Containing Adamantane Derivatives**

927C0333B Moscow *KHIMIKO-FARMATSEVTICHESKIY ZHURNAL* in Russian Vol 25 No 7, Jul 91 (manuscript received 06 Jul 90) pp 49-51

[Article by Yu. N. Klimochkin, I. K. Moiseyev, O. V. Abramov, G. V. Vladyko, L. V. Koeobchenko and Ye. I. Boreko, Kuybyshev Polytechnical Institute; Belorussian SSR Scientific Research Institute of Epidemiology and Microbiology, Minsk; UDC 615.281.8:547.592.1].012.1]

[Abstract] Cursory details are presented on the synthetic rationale employed in the preparation of 16 thiocarbamate, selenocarbamate, sulfamide, dithiocarbamate and isothiocyanate congeners of adamantane as part of screening for novel antivirals. Tissue culture trials showed that 12 of the agents possessed some degree of antiviral activity against selected viruses in the following group: herpes simplex 1, vaccinia, fowl plague, RSV, VSV, VEE or ECHO-6. These observations indicate that further assessment of this class of adamantane congeners for antiviral activity is warranted. Tables 2; references 9: 5 Russian, 4 Western.

**Effects of Opiate Agonists on Myocardial Energetics in Rats With Hemorrhagic Shock**

927C0329A Moscow BYULLETEN

EKSPERIMENTALNOY BIOLOGII I MEDITSINY

in Russian Vol 111 No 5, May 91 (manuscript received 18 Jun 90) pp 469-471

[Article by V. D. Slepshkin and Yu. Gressler, Chair of Anesthesiology and Resuscitation, Novokuznetsk Institute of Advanced Training of Physicians; Institute of Pathologic Biochemistry, Dresden Medical Academy; UDC 616-006:615-001.36]-092.9-07:616.127-008.989.6:577.124.7]-02:615.31:[547.943:547.95]

[Abstract] Hemorrhagic shock in 320-350 g male Wistar rats was employed as an experimental model for assessing potential therapeutic application of opiate agonists in such conditions. The trials were performed on rats under sodium pentothal anesthesia (50 mg/kg; i.p.) subjected to fractionated blood loss amounting to the 30 percent of circulatory volume. In the course of the hemorrhage and in the posthemorrhagic state the animals were treated intravenously with 100 µg/kg of the following leu-enkephalin congeners: D-Ala<sup>2</sup>-D-Leu<sup>5</sup> (I), D-Ala<sup>2</sup>-N and Phen<sup>4</sup>-Gly<sup>5</sup> (II) and D-Ala<sup>2</sup>-Arg<sup>6</sup> (dalargin). Blood pressure monitoring demonstrated that compound II and dalargin were particularly effective in maintaining arterial blood pressure 20-30 percent higher than the levels in untreated animals during and after hemorrhage. In addition, the enkephalin analogs also precluded a drastic drop in myocardial levels of ATP, ADP and the ATP/ADP ratio to the extent seen in untreated rats. Dalargin was also the sole enkephalin effective in maintaining myocardial creatine phosphate at a higher level than seen in untreated controls and rats treated with I and II. These findings show that agonists of endogenous opiates may have therapeutic potential in hypovolemic shock. Compound II, a µ receptor agonist, was particularly effective during hemorrhage, while compound I, a δ receptor agonist, was most effective in promoting recovery of baseline blood pressure in the posthemorrhagic period. Tables 2; references 9: 1 Romanian, 5 Russian, 3 Western.

**Facilitated Extinction of Exploratory Activity as Indication of Nootropic Action**

927C0329B Moscow BYULLETEN

EKSPERIMENTALNOY BIOLOGII I MEDITSINY

in Russian Vol 111 No 5, May 91 (manuscript received 29 Jun 90) pp 498-500

[Article by R. U. Ostrovskaya and T. A. Gudasheva, Laboratories of Psychopharmacology and of Chemistry of Heteroatomic Structures, Institute of Pharmacology, USSR Academy of Medical Sciences; UDC 615.214.3:547.745].015.4.07]

[Abstract] Piracetam, a well established nootropic, and a series of its pyroglutamic acid and proline congeners were tested for impact on extinction of exploratory activity in outbred albino mice to determine whether this behavioral parameter can serve as an indicator of nootropic action. Monitoring of the locomotor behavior demonstrated that in all cases extinction was facilitated with much smaller doses than required in passive avoidance tests, e.g., 12.25 mg/kg

vs. 200 mg/kg in the case of piracetam (route of administration unspecified). Accordingly, the simple test for impact on the rate of extinction of exploratory behavior can be utilized in assessing nootropic action of drugs lacking sedative side-effects. Figures 2; tables 1; references 10: 8 Russian, 2 Western.

**Experimental Assessment of Oxygen Capacity of Modified Polyhemoglobin in Extreme Dilution Models**

927C0329C Moscow BYULLETEN

EKSPERIMENTALNOY BIOLOGII I MEDITSINY

in Russian Vol 111 No 5, May 91 (manuscript received 12 Jul 90) pp 503-505

[Article by I. R. Kolonina, Yu. A. Litvinenko and A. V. Sokolov, Laboratory of Pathologic Physiology, All-Union Hematologic Scientific Center, USSR Ministry of Health, Moscow; UDC 615.384:547.963.4].036.8.076.9]

[Abstract] Polyhemoglobin supplemented with pyridoxal-5'-phosphate (PH/PP) was further assessed for its oxygen carrying capacity in exsanguinated 11.3 kg outbred dogs. Monitoring of arterial and venous oxygen tensions showed that intravenously administered 10 percent PH/PP accounted for 75-80 percent of the oxygen carrying capacity of the blood when the hematocrit fell to 5 percent or below. This capacity was sufficient to ensure 100 percent 4 hour survival despite a two-fold reduction in arterial and venous oxygen levels. Intravenously transfused 10 percent rheopolygucan did not possess sufficient oxygen carrying capacity to support life under analogous conditions. Figures 1; tables 2; references 12: 3 Russian, 9 Western.

**Intracerebral Microdialysis in Assessment of Effects of Atypical Neuroleptics and Anxiolytics on Release and Metabolism of Striatal Dopamine in Wakeful Rats**

927C0329D Moscow BYULLETEN

EKSPERIMENTALNOY BIOLOGII I MEDITSINY

in Russian Vol 111 No 5, May 91 (manuscript received 05 Jun 90) pp 505-507

[Article by M. B. Bogdanov, R. R. Faynetdinov, V. S. Kudrin, O. S. Medvedev and A. V. Valdman (dec), Scientific Research Institute of Pharmacology, USSR Academy of Medical Sciences, Moscow; UDC 612.82.015:577.175.82].014.46:615.214.2].085.1]

[Abstract] Intracranial microdialysis was employed in further assessment of the mechanism of action of selected neuroleptics and anxiolytics on striatal dopaminergic mechanisms. Studies on wakeful 250-300 g male Wistar rats demonstrated that risperidone, sulpiride and buspirone as antagonists of D<sub>2</sub>-type dopamine receptors enhanced extracellular levels of dopamine, dihydroxyphenylacetic acid (DOPAC) and homovanillic acid (HVA). Ritanserin, an antagonist of 5-HT<sub>2</sub>-type serotonin receptors, was without effect on dopamine secretion from the striatum and less effective than the previous three agents in enhancing release of DOPAC and HVA. 5-Methoxy-N,N-dimethyltryptamine, a nonselective agonist of 5-HT<sub>1</sub> receptors, was entirely without effect on striatal dopamine, DOPAC and HVA metabolism. Tables 1; references 15: Western.

### Revitalization of Pharmaceutical Industry Urged

927C0252A Moscow DELOVOY MIR in Russian  
4 Dec 92 p 3

[Article by Ninel Dmitriyeva: "How Is Pharmacy Revived?"]

[Text] The phone rang in the apartment early in the morning. A telegram had been received from Kirov. A friend who had undergone a serious oncological operation was urgently needing the drug "timogen." I could not sleep. I sat by the telephone. At first I did not pick up the handset. Clearly no one was there. Then frequent beeps could be heard or else the answers: "No, it has not come in."

Dropping all other matters, I went to the "Farmatsiya" Association. They fidgeted with the telegram and sympathized. They explained that thousands of patients undergo operations in hospitals daily. And timogen is needed to improve their immunity and restore resistance of the organism in the post-operative period. There was not enough. And now, unfortunately, there was not any. In the Russian "Farmatsiya" Association, I found M. Vorontsova, deputy chief of the division of organizing medical support. Looking at me with clear eyes, she soothed:

"We have sent timogen to all cities. It is available at the Kirov central warehouse. I will dispatch an order to them, and the medicine will be sent to the hospital for your friend." Sincerely thanking her, I left relieved; there are sympathetic people.

A few days later, I was told that there was no timogen in the Kirov warehouse. St. Petersburg had come to the rescue, and three packages had been sent to Kirov.

Drugs... They are in disastrously short supply these days. At a clinic in Alma-Ata, a critically ill patient was being given cardiac glycosides, but they ran out. Another drug was substituted, but it was contraindicated, and the patient developed edema. She could not be saved. "First Aid" is suffering as well: There is a shortage of medicine and equipment. The problem is especially acute for saving victims of poisoning.

What can the drug stores offer? There is no analgin, mustard plaster, iodine, medicinal herbs or other simple medicines. At Moscow drug store N404 I was shown a planned drug order had come back from the medical warehouse. More than half of the order could not be met, and some of the medicines had been substituted with analogs having contraindications; still, of course, there was a general schedule of allocations: several "hot" items were added with limited expiration dates, besides having many side effects and contraindications, such as, for example, an imported schizophrenia agent moditen-depo. It was once purchased for cash in Yugoslavia. It has been distributed by mandatory procedure to drug stores where it generally sits idly on the shelf.

There is a surplus of medicines like the Yugoslavian case in medical warehouses. In exchange, some are so scarce that you could not find them in broad daylight even with a lantern... Unfortunately, there is a greater shortfall in the supply of medicines for the needs of public health with each passing year. In 1985, the supply of medicines to the people of our nation was 52 percent of demand, in 1985 it was 39 percent, and in 1991, even less.

There are many reasons for this. Several chemical and pharmaceutical plants have been closed because of ecological conditions. And the pharmaceutical factories still in operation are working at half load because of shortages of raw materials and antiquated equipment. There is also a shortage of glassware. Nothing is being done about organizing its reception, though it is long overdue.

It should also be taken into consideration that the modest range of drugs produced here includes some that are prohibited in other nations. An example is "Levomycetin" (highly toxic). There are also many obsolescent drugs: besalol, calcex, urotropin, klofelin, riboksin and others.

To be fair, it must be said that our government is trying to find a way out of the difficult situation with regard to providing medicines in our nation. A few years ago, an enactment was passed on building 37 drug producing plants, but not one has been built. Either local councils have not allocated property, or they are haggling, demanding inconceivable appropriations. Funds have been set aside for purchasing imported drugs. Half of our medicines are purchased internationally both in rubles and for foreign currency. However, every imported pill is five to seven times as expensive as what is produced here.

Some might say that we would do better to try to get by without imported drugs. Yes, we have a number of scientific research institutes that long ago developed several new modern drugs, but they are not being put into production. We have neither the money nor the appropriate equipment. Dozens of scientists are away working on contract for other nations, and hundreds have emigrated. While drug production here has fallen into complete decay, the U.S. pharmaceutical industry is increasing production by 10 percent per year. Every five years, medicines are replaced with more effective ones.

Let us return to our nation, which has fallen apart into sovereign republics. Economic ties and agreements are being broken. Planning and material-technical supply leaves a lot to be desired. There has been a decline in medical imports. The USSR has an indebtedness for their redemption not only for 1991, but for 1990 as well.

Of course, we must eliminate our debt on payment for imported prepared medicines as soon as possible, provide for allocation of cash appropriations to purchase prepared medicines, raw materials and supplies, equipment and spare parts for drug production. Perhaps we should set up a state-wide regulatory agency that would make it incumbent on suppliers to ship raw materials and supplies to enterprises regardless of their agency jurisdiction.

In the Russian Ministry of Public Health, it is assumed that "Soyuzfarmatsiya" and "Soyuzmedtekhnika," which handle foreign economic deals, should not be union associations, but rather independent cost accounting associations that would work in the interests of any partner. The RSFSR is ready to assume the responsibility of supply coordinator. We do not need a pharmaceutical committee in the form in which it now exists.

It would not hurt to recall the age-old experience of folk medicine: herbal treatment. Western nations gave these medicines the green light long ago.



The transition to a market economy has given rise to the need for alternative drug stores: leased, joint-stock, privately owned. Their purpose is to help people use medicines rationally. Privatization of drug stores will help them to get out from under the system of the Ministry of Public Health, and their functions will be turned over to the management of local councils. Such drug stores will be able to make independent use of the payroll fund and hire skilled specialists. No general schedule of allocations will force them to carry unnecessary medicines. They themselves will determine their own selection of products, placing orders with medical warehouses and even with pharmaceutical companies for medicines that are in demand and that correspond to the latest advances in modern pharmacology.

To attract clients, drug stores of this kind could offer additional services for a nominal fee: tests for diabetes, high blood pressure, glaucoma. Consultative stations could be set up where customers could get the advice of a pharmacist. If a computer were installed in the drug store, it could be used to keep track of medicines prescribed for clients, preventing the possible danger of combined action of drugs. The computer in the drug store could take the pharmacist's place in preparation of complex prescriptions. In future there would be a real possibility of entry of the drug store into the international market.

It would also be effective to change the structure of production of medicines, merging pharmaceutical and chemical enterprises into associations and companies, transforming the entire cycle of drug production from initial development to manufacturing and distribution. One would like to believe that revitalization of Soviet pharmacy is not far off.

#### **Pigment Used As Radiation Injury Treatment**

927C0252B Moscow ROSSIYSKAYA GAZETA in Russian  
16 Jan 92 p 6

[Article by Manya Nikolayeva: "Mummy Against Radiation"]

[Text] The Chernobyl accident resulted in elevated irradiation of thousands of people. Medicine has become aware of unique curative properties of mummy [pigment] that may help in the treatment of such patients. This is what our correspondent was told by the head scientist of the department of radiochemistry at Moscow State University, Doctor of Chemical Sciences Yuriy Dmitriyevich Perfilov:

"Chemical scientists have already taken the first step on the path to discovery of a reliable method of treating victims of radiation by using mummy. First, we looked at the reaction of mummy with iron and cobalt. As you know, iron is a component of blood and acts as a transporter of oxygen in the form of intricate biocomplexes, but radiation breaks links in the chain of chemical bonds, including iron-containing bonds that perform vitally important functions.

"Now it has been scientifically proven that 'mountain balm' readily interacts with iron, producing compounds of various types. Apparently, mummy is capable of reconstructing damaged sections of biological objects, as well as blocking harmful substances that arise under the action of radiation."

#### **Stress Epidemic in Chernobyl Victims**

927C0252C Moscow PRAVDA in Russian 14 Dec 92 p 2

[Article by Professor I. Brekhman, Chairman of Committee on Investigation of Medicinal Agents of the Far East, Far Eastern Department, USSR Academy of Sciences, Vladivostok, "Stress Epidemic: Echo of Chernobyl"]

[Text] At the time of the advent of nuclear weapons, biomedical science was not ready for prevention and treatment of radiation accidents, and was still unprepared when the accident occurred at Chernobyl Nuclear Electric Power Plant. Even back in the fifties, in general research on the universal protective (adaptogenic) properties of ginseng and eleuthero-coccus together with G. M. Mayanskiy and V. A. Matyukhin, we were studying their radiation protective action.

During the early months of cleanup at Chernobyl, eleuthero-coccus was used rather extensively. The problem of protecting hundreds of thousands of people from radiation in various regions of Belarus, the Ukraine and Russia is increasing in urgency and scale with each passing year.

In this context, it must be borne in mind that people are suffering not only from radiation itself, but from stress as well. Stress from not believing that they are being told the whole truth, from continual and justified radiophobia, inadequate and low-quality nutrition, unsatisfactory medical care, and from a host of other things. All these factors, including radiation action itself, are causes of stress acting over the course of several years. As a result, the combined stress covers hundreds of thousands of people. Chernobyl is a stress epidemic.

Following the Chernobyl accident, as after earthquakes, floods, and other natural disasters, people were in what is called a reactive state that alters human responses and behavior. Chernobyl contingents have been remaining in affected centers for six years now... People are still under stress from contradictory and unreliable information, social stigma, and much more.

Nutrition in the disaster zone should not only be rich in protein, vitamins and other indispensable components, but should be free of oxidized fats, and contain substances that prevent processes of oxidation: natural antioxidants. This is important because after radiation action, peroxide products accumulate in the organism: radiotoxins. Workers at our institute have established accumulation of these same substances under any form of stress, prompting us to call them "stressines."

Finally, so-called medicines for the healthy should be extensively used. Actually, these are medicines for people in an intermediate state between sickness and health. Under ordinary present-day conditions, from 60 to 80 percent of all people are in this "third" state. The figure is certainly still higher in radiation zones.

Our department of problems of regulating biological processes of the Pacific Oceanological Institute of the Far Eastern Department, USSR Academy of Sciences, over the past 40 odd years has created a number of natural medicinal agents that increase the general resistance of the human organism to various unfavorable factors. Considering a certain prejudice against drugs, we turned our attention to the creation of natural food additives and products of



elevated biological value: all this may be used not only in zones around Chernobyl, but also in other regions where the ecological situation is bad.

Among the entire set of substances, the most extensively studied and widely tested is the far eastern spiny eleuthero-coccus. The roots, stems and leaves of the plant are used. A root extract has universal stress-projector and adaptogenic action and is widely used as a prophylactic agent. With repeat course doses over a number of years, its effect increases. Use of eleuthero-coccus root extract in periodic courses by three thousand truck drivers of AvtoVAZ over a six-year period reduced the sick rate for flu, hypertonic and ischemic heart disease by a considerable factor. The preparation has prophylactic and curative action in chronic radiation effects. The roots and leaves of the eleuthero-coccus can be used as special kinds of tea, the nonalcoholic beverages "Bodrost," "Baykal" and "Gornyy klyuch."

While alcohol is extremely undesirable, it is, of course, used in the stricken zones. Ordinary vodka should be replaced with vodka to which eleuthero-coccus "Zolotoy rog" or kaprim "Zolotoye runo" has been added. Replacement of ordinary vodka with "Zolotoye runo" in one region of the North while retaining all other alcoholic beverages for 10 months reduced the total consumption of alcohol by 28 percent.

Kaprim also has good stress-projector and adaptogenic action. Of the medicinal agents that we introduced, rantarin from the antlers of northern deer may be used. A considerable improvement in health can be achieved by partial (up to 50 percent) replacement of white sugar with unrefined, so-called brown sugar. It does not have the disadvantages of the refined variety, and moreover has a number of useful properties. A monograph covering years of research on brown sugar has been published in Britain ("Pergamon Press") and in Leningrad ("Nauka").

In the foregoing we have mentioned medicinal agents, food additives and products of elevated biological value whose production is permitted by appropriate technical documentation. But... except for the extract of eleuthero-coccus roots, rantarin and "Baykal," none of the other products is being produced by industry, not even brown sugar, which might be a health benefit to people on the scale of the entire nation.

Our team has done work on several other projects, either finished or in the stage of research, and much more effort is needed lest we throw up our hands in despair at the hopeless trouble of getting such needed natural medicines to the people.

**Biological Aspects of Low-Dose Radiation**

927C0285A Moscow *RADIOBIOLOGIYA* in Russian  
Vol 31 No 3, May-Jun 91 (manuscript received 25 Jan 91)  
pp 318-325

[Article by V. Ya. Gotlib, I. I. Pelevina, Ye. F. Konoplya, A. A. Alferovich and A. A. Konradov, Institute of Chemical Physics, USSR Academy of Sciences, Moscow; Institute of Radiobiology, Belorussian SSR Academy of Sciences, Minsk; UDC 577.391]

[Abstract] Experiments were designed to monitor the late sequelae of low-dose radiation, using HeLa cells subjected to 10, 20 or 40 cGy dose  $\gamma$ -irradiation. Distribution

analysis demonstrated that with time reproductive functions of progeny cells are impaired giving rise to an increase in the number of colonies with low cell counts and presence of giant cells. This phenomenon is dose-related with the impairment first evident after ca. six generations in the 10 cGy group and nine generations in the 20 cGy groups. More than 12 generations are required for similar manifestations in the 40 cGy group. These observations demonstrated that the effects of low-dose radiation may require several generations for manifestation, indicating that in human cases of irradiation monitoring should encompass descendants. Figures 5; references 19: 5 Russian, 14 Western.

### Polymeric Peptide Vaccine Against Foot-and-Mouth Disease Virus

927C0285B Moscow BIOORGANICHESKAYA KHIMIYA in Russian Vol 17 No 7, Jul 91 (manuscript received 09 Apr 90; in final form 05 Sep 90) pp 953-963

[Article by A.V. Pavlov, S.S. Rybakov, V.N. Ivanyushchenkov (dec), A.V. Chepurkin, V.N. Petrov, N.N. Drygalin and A.N. Burdov, All-Union Scientific Research Institute of Foot-and-Mouth Disease, Vladimir; UDC 578.112.083.3:578.835'224:615.371]

[Abstract] Conventional peptide chemistry was utilized in the synthesis of polymeric analogs of the 14 amino acid VP<sub>1</sub> (142-155) peptide of foot-and-mouth disease virus (FMDV). The resultant products showed a weight distribution on exclusion chromatography of 34, 30, 23, 20 and 10 KD, and were tested for immunogenicity on susceptible animals. Intramuscular immunization of rabbits with 100 µg showed that all fractions elicited neutralizing antibodies, while two-fold intramuscular vaccination of guinea pigs with 20 µg ensured 100 percent survival on challenge with FMDV. Best survival rate with two 400 µg immunizations of the monomer was < 20 percent. Trials on cattle—representing highly susceptible animals—with various dosages showed that two immunizations administered succutaneously ensured a 70 percent survival rate on subsequent inoculation with FMDV. These findings demonstrate that linear polymerization of a viral peptide significantly enhanced its immunogenicity and suggests yet another approach in the construction of viral vaccines. Figures 1; tables 5; references 16: 4 Russian, 12 Western.

### Cloning of *Streptococcus bovis* α-Amylase Gene and Its Expression in *Bacillus subtilis* Cells

927C0336A Moscow MOLEKULARNAYA GENETIKA, MIKROBIOLOGIYA I VIRUSOLOGIYA in Russian No 6, Jun 91 (manuscript received 17 Jul 90) pp 19-21

[Article by P. Yavorski, M. M. Kuntsova, Ye. F. Loseva, and F. K. Khasanov, Farm Animals Institute, Czechoslovakian Academy of Sciences, Koshitse, Czechoslovakia; General Genetics Institute, USSR Academy of Sciences, Moscow; UDC 579.862.1:[579.222:577.152.321]:579.253; 579.852.11]

[Abstract] This paper describes a procedure for cloning the α-amylase gene from *Streptococcus bovis* AO24/85 and investigates expression of this enzyme in *Bacillus subtilis* cells. Two approaches were employed to isolate the α-amylase gene from *S. bovis*. The first, which involved the marker rescue phenomenon, was unsuccessful due to the structural instability of the recombinant plasmids in the *B. subtilis* cells. The second involves the use of plasmid pMX39. One clone out of 3,900 transformants was obtained that formed a starch hydrolysis zone around itself. The cloned insertion of DNA was found to bear unique restriction sites for EcoRI, EcoRV, PvuII, and two SalCI sites. Hybridization experiments on nitrocellulose filters were performed to determine the nature of the cloned fragment. cDNA from *B. subtilis* RUB834 and *S. bovis* AO24/85 was restricted with EcoRI. The restricts were then subjected to electrophoresis in 0.8 percent agarose gel and hybridized with two EcoRI fragments from plasmid pJK108 bearing sequences of cloned DNA. The results suggest that the

cloned DNA fragment bearing the gene for α-amylase is of *Streptococcus* origin. Investigation of the biochemical parameters of the α-amylase enzyme from *S. bovis*, that is synthesized in *B. subtilis* under the control of the cloned gene revealed that there is approximately 80 percent α-amylase activity in the cultural fluid in the cultivation of chimeric *B. subtilis* cells. It was also shown that α-amylase was most active at 55°C. In conclusion, the results demonstrated that *S. bovis* bacteria cloned in *B. subtilis* can express the α-amylase gene. Figures 3; references 21: 3 Russian, 18 Western.

### Investigation of Antigenic Structure of Glycoprotein E1 From Venezuelan Equine Encephalomyelitis Virus Using Monoclonal Antibodies

927C0336B Moscow MOLEKULARNAYA GENETIKA, MIKROBIOLOGIYA I VIRUSOLOGIYA in Russian No 6, Jun 91 (manuscript received 12 Jul 90) pp 21-24

[Article by I. A. Razumov, Ye. V. Agapov, A. V. Pereboyev, Ye. V. Protopopova, S. D. Lebedeva, and V. B. Loktev, All-Union Scientific Research Institute of Molecular Biology, Vektor Scientific Production Association, USSR Ministry of the Medical Industry, Novosibirsk Oblast, Koltsovo; UDC 578.833.26:[578.224:577.112.853]:578.74.083.3]

[Abstract] This paper presents data on a more complete description of the antigenic structure and function of glycoprotein E1 from Venezuelan equine encephalomyelitis virus, strains Trinidad, TC-83, and TC-230 and Eastern equine encephalomyelitis virus. Female Lou rats (180-200 g) were immunized twice at a two-week interval with an intraperitoneal injection of 10 µg of purified Venezuelan equine encephalomyelitis virus. From 19 independent hybridizations of rat myeloma 210 RC Y3-Ag 1.2.3 cells, 623 hybrid lines were obtained capable of growing on a selective medium with aminopterin. Seventeen hybridomas were finally found that secreted monoclonal antibodies that reacted with protein E2; four were found that secreted monoclonal antibodies specific for protein E1. Murine hybridomas based on murine myeloma Pe 10S1/1-Ag 4.1 cells were employed to perform five hybridizations. From them 46 hybridomas were selected that secreted monoclonal antibodies to Venezuelan equine encephalomyelitis virus. Immunoblotting was then used to select four hybridomas that produce monoclonal antibodies that react with glycoprotein E1. It was shown that none of the eight monoclonal antibodies to protein E1 displayed virus-neutralizing activity in a cell culture. However, monoclonal antibodies 8D2 displayed a protective effect and were able to protect animals from the administration of 1-2 million LD<sub>50</sub> of the virulent Trinidad strain. The mechanism of this protection is attributed to the antibody-dependent lysis of the infected cells or blockage of virus replication in the macrophage system. Three monoclonal antibodies were found that reacted with Eastern equine encephalomyelitis virus. Competitive solid phase radioimmunoassay between <sup>125</sup>I-labeled and unlabeled purified monoclonal antibodies was performed for more detailed mapping of monoclonal antibody binding epitopes for protein E1. In conclusion, a collection of eight hybridomas that secrete monoclonal antibodies to

Venezuelan equine encephalomyelitis virus glycoprotein E1 was developed. Figures 2; tables 2; references 24: 3 Russian, 21 Western.

### Conjugation and Microencapsulation of Antigens

927C0351A Moscow VOPROSY VIRUSOLOGII  
in Russian Vol 36 No 4, Jul-Aug 91 pp 346-347; UDC  
615.371.014.6.012]

[Text] It is becoming increasingly more obvious in recent years that complexing of synthetic polymers with viruses or bacterial antigens makes it possible to significantly intensify the immunizing properties of the latter<sup>1-3</sup>. This phenomenon is observed both with covalent bonding of antigens with polymers, and with encapsulation of antigens in spherical polymer particles. In the case of covalent bonding with polymers, which play the role of a biologically active immuno-adjuvant, weakly antigenic proteins of various origin transform into highly immunogenic preparations. Combination of both weak and relatively strong standard T-dependent antigens with polymer stimulators makes it possible to obtain strong T-independent immunogens that induce production of antibodies against the corresponding epitopes. Conjugation with polymers also makes it possible to reduce the immunizing doses of antigen.

The principle of creating vaccinating complexes with polyions has been confirmed in work with both bacterial and viral antigens<sup>2</sup>. In particular such complexes were obtained with different structural proteins of the influenza virus; in this case by covalent bonding of hemagglutinin<sup>2</sup> and protein M of influenza virus with synthetic polyions, it was possible to sharply raise their immunogenic activity<sup>1</sup>.

The next step in using synthetic polymers in vaccinology is microencapsulation of bacterial and viral antigens in them. The polymer is prepared in the form of spherical particles from 1 micron to 3 millimeters in size, in which isolated viral antigens or whole viral particles are contained<sup>4,5</sup>. In this case the polymer forms a protective shell for the antigen for a given period of time. When used orally, encapsulated antigens are protected against the low pH of gastric juices, bile acids and their salts, and proteolytic enzymes of the intestinal tract.

Polymers that are biodegradable in the body and which are used in pharmaceutical industry and in surgery are of the greatest interest to the purposes of microencapsulation. One such synthetic polymer approved for medical practice is the copolymer polylactide-polyglycolide (PL-PG) which breaks down gradually in response to hydrolysis of ether bonds to lactic and glycolic acids—that is, to ordinary components of the body. It is used in pharmaceutical industry to prolong the action of medicinal agents and hormones, and in surgery to prepare implants that are resorbed over a given time period. The polymer is biologically compatible, and it does not elicit any noticeable inflammatory reactions at the introduction site. The rate of hydrolysis of the polymer particles, and consequently the rate of release of viral antigen encapsulated within them, can be programmed by mixing polyglycolide with polylactide in different proportions. In particular, antigen is released on the 30th day after administration from particles prepared with a PL:PG ratio of 50:50, and on the 130th day when the ratio is 100:0. When these particles are administered together, antigen is released from them in two pulses following the indicated

time periods. By combining particles made with different PL:PG ratios into a single mixture we can make a vaccine preparation which will release antigen, for example, 10, 130 and 210 days after one-time subcutaneous injection. A copolymer can be prepared in this manner such that antigen would not be released until 2 years after injection. Consequently microencapsulated vaccines can simulate three- to four-time antigenic stimulation at prescribed intervals after a one-time injection.

A special merit of the polymer is its ability to dramatically potentiate the immune response to encapsulated antigen. In particular, when the latter is injected into experimental animals, antibody production grows by 500 times. An adjuvant effect of the polymer equal to the effect of Freund's adjuvant is observed with encapsulation of bacterial or viral protein or glycoprotein, and of whole viral particles.

The ability to penetrate into mucous membranes of the intestinal and respiratory tract with oral or tracheal administration respectively, followed by induction of local and general immune reactions, is an important property of synthetic polymers.

It has been established that when administered orally, particles less than 10 microns in size are internalized by cells covering Peyer's patches, followed by their penetration into macrophages—that is, into antigen-presenting cells. Secretory IgA and circulating IgG cells are induced in this case. Similar results were obtained with intratracheal administration of encapsulated bacterial anatoxin.

The described properties of synthetic polymers make them especially attractive in regard to designing vaccines out of polypeptides obtained by genetic engineering or by synthetic methods.

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### Miscellaneous

#### Photometric Determination of Sodium and Cesium Iodides in Workplace Air

927C0330A Moscow GIGIYENA TRUDA I  
PROFESSIONALNYYE ZABOLEVANIYA in Russian  
No 9, Sep 91 (manuscript received 9 Oct 90) pp 36-37

[Article by A. V. Gorelova, I. L. Gerasimova, and A. I. Fadeyev, Medical Academy imeni I. M. Sechenov, Moscow; UDC 613.632.4:[546.311'15]-073.524]



[Abstract] Cesium and sodium iodides, white or light-yellow water-soluble crystalline powders used in the manufacture of spectrometry equipment, are found in the air as aerosols. This paper reports the development of a photometric technique for measuring those iodides in the air of the workplace. The technique is based on the oxidation of negative I ions with bromine water, the interaction of the isolated iodine with an excess of potassium iodide in an acidic medium, with subsequent formation of complex  $I_3$  ions and photometric measurement of the reaction product at wavelengths of 350-365 nm. The technique has a sensitivity of  $5 \mu\text{g I}^-$  per sample. The range of measurable concentrations is 0.2-50  $\text{mg/m}^3$ . References 3: Russian.

**Gas-Chromatographic Determination of Dichlorpinacolin in Workplace Air and in Water**

927C0330B Moscow GIGIYENA TRUDA I  
PROFESSIONALNYYE ZABOLEVANIYA in Russian  
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[Article by Kh. T. Asilbekova, V. M. Khasanova, Institute of Chemistry, Uzbek Academy of Sciences, Tashkent; UDC 613.632:615.282]-074]

[Abstract] Dichlorpinacolin (DCP)—a pungent, white crystalline substance with a boiling point of  $50^\circ\text{C}$ , a solubility in water of 140  $\text{mg/l}$  at  $20^\circ\text{C}$ —is the raw material for producing the fungicides triadimenol and azocene. The maximum permissible concentration in workplace air is  $5 \text{ mg/m}^3$ , in water 0.05  $\text{mg/l}$ . In developing sensitive gas-chromatographic techniques to detect DCP, the researchers used a Tsvet-24 chromatograph with a constant recombination rate detector on three packed columns two meters long, with an inside diameter of three mm, with SE-30.3 percent (I), OV-17.3 percent (II), and Carbowax 1500.5 percent (III), and a solid carrier of Inerton-Super with particles 0.16-0.20 mm in diameter. The lowest threshold for determining DCP in the sample volume was 0.001  $\mu\text{g}$ ; in the air,  $2.5 \mu\text{m}^3$ , and in the water, 0.025  $\text{m/l}$ . Measurable concentration range in the air was 2.5-40.0  $\mu\text{m}^3$  (for I and III) and 2.5-30  $\mu\text{m}^3$ ; in water, 0.025-0.4  $\mu\text{l}$  (I, III) and 0.025-0.3  $\mu\text{l}$  (II). Absolute calibration techniques were used for the quantitative assessments. Figures 1, references 1: Russian.

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